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PENICILLIN IN SUBACUTE BACTERIAL ENDOCARDITIS

REPORT TO THE MEDICAL RESEARCH COUNCIL ON 269 PATIENTS TREATED IN 14 CENTRES APPOINTED BY THE PENICILLIN CLINICAL TRIALS COMMITTEE

BY

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Secretary of the Committee

Between February, 1945, and March, 1946, 269 patients suffering from subacute bacterial endocarditis were treated in the 14 centres appointed by the Medical Research Council in Belfast, Birmingham, Bristol, Cardiff, Edinburgh, Glasgow, Leeds, Liverpool, London (St. Mary's, Middlesex, and St. Bartholomew's Hospitals), Manchester, Newcastle-upon-Tyne, and Sheffield. The patients were unselected, and were investigated and treated according to a co-ordinated plan.

Results in Previously Untreated Cases

When this investigation was first planned not only was penicillin scarce but very few cases of recovery had been described, and for these reasons amounts of penicillin were used which are now known to be inadequate.

The first group of 52 patients received a total of 5 million units, but the daily dose was varied (Table I). This experiment clearly showed that, within these limits of dosage, the duration of treatment was of greater importance than the amount of penicillin given daily—a conclusion which may now be a commonplace but which at that time was of some importance.

TABLE I.—*Patients Receiving a Total of 5 Million Units of Penicillin, Given in Courses of 5, 10, and 20 Days. (No case had previously received penicillin)*

Dose	Total No. Treated	Died with Infection Apparently Controlled	Died with Infection Uncontrolled	Relapsed	"Cured"	Average Follow-up (Days)	Relapsed or Died Infected
1 mega unit for 5 days ..	18	3	2	13	0	—	83%
0·5 mega unit for 10 days ..	16	4	0	8	25%	665	50%
0·25 mega unit for 20 days	18	6	0	4	44%	579	22%

In the next group of 158 patients the duration of treatment was established at 28 days, but the daily dose was varied (Table II). Of 17 patients who received 100,000 units a day for 28 days, 7 (41%) relapsed or died infected. Of 83 patients receiving 250,000 units a day for 28 days, 13 (16%) relapsed or died infected. Of 58 patients who received 500,000 units a day for 28 days, 4 (6.9%) relapsed or died infected. Only occasionally can failure be explained on the basis of a highly resistant organism; in the four failures referred to above the coefficient of resistance expressed as a multiple of that of the Oxford staphylococcus was 2, 2, 6, and 32.

TABLE II.—*Patients Treated for 28 Days with a Daily Dose of 0.1, 0.25, and 0.5 Mega Unit. (No case had previously received penicillin)*

Dose	Total No. Treated	Died with Infection Apparently Controlled	Died with Infection Uncontrolled	Relapsed	"Cured"	Average Follow-up (Days)	Relapsed or Died Infected
0·1 mega unit a day ..	17	4	0	7	35%	579	41%
0·25 mega unit a day ..	83	30	2	11	48%	447	16%
0·5 mega unit a day ..	58	22	3	1	55%	423	6·9%

Twenty-two previously untreated patients received other systems of dosage, and the results in this group, although not instructive from a therapeutic point of view, are shown in Table III.

TABLE III.—*Patients Receiving Courses not Included in Tables I or II. (No case had previously received penicillin)*

Dose	Total	Died with Infection Apparently Controlled	Died with Infection Uncontrolled	Relapsed	"Cured"	Average Follow-up (Days)
0·25 mega unit a day for from 5 to 6 weeks	3			1	2	426
0·5 mega unit for 21 days	11	1		2	8	650
0·5 mega unit for 5 weeks	4	2			2	341
0·5 mega unit for 2 weeks, increased to 1 mega unit for 2 weeks	4		1		3	395

Except in a few cases penicillin was given either by three-hourly injection or by continuous intramuscular infusion. No difference in the therapeutic results can be demonstrated, and opinion on the merits of these two methods is divided. In some cases the dosage given was only approximately as stated; these exceptions were indicated in a previous report in the *British Medical Journal* of March 16, 1946 (p. 381).

Relapses

Patients who have relapsed are in a separate category with regard to both treatment and prognosis. Of 42 patients who had relapsed after a long course of treatment 59% again relapsed or died infected (Table IV): it can be calculated from Tables I, II, and III that had these patients not previously been treated unsuccessfully only 14% would have been expected to relapse or die infected. Patients who relapse after a short course of penicillin also appear to be slightly more resistant to subsequent treatment (Table V).

The conclusion is justified that if a patient does not respond to a course of penicillin he is less likely to respond to a second course. This may mean that resistance of the

TABLE IV.—*Patients Previously Treated with a Course of Penicillin, of 20 Days or More*

Dose	Total No. Treated	Died with Infection Apparently Controlled	Died with Infection Uncontrolled	Relapsed	"Cured"	Average Follow-up (Days)	Relapsed or Died Infected
0·5 mega unit for 10 days ..	2			2			100%
0·25 mega unit for 20 days	5		4		1	540	80%
0·25 mega unit for 28 days	10	1	3	5	1	551	80%
0·5 mega unit for 20 days ..	4		3		1	394	75%
0·5 mega unit for 28 days ..	17	4	4	3	6	411	41%
0·5 mega unit for 6–8 weeks	4	2	1		1	270	25%
Total	42	7	15	10	10		59%
Expected numbers from Tables I, II, and III		14·1	1·3	4·5	22		14%

TABLE V.—*Patients Previously Treated with only a Short Course of Penicillin, of 5 to 10 Days' Duration*

Dose	Total No. Treated	Died with Infection Apparently Controlled	Died with Infection Uncontrolled	Relapsed	"Cured"	Average Follow-up (Days)	Relapsed or Died Infected
1 mega unit for 5 days ..	1			1			
0·5 mega unit for 10 days ..	2				2	631	
0·1 mega unit for 28 days ..	4		1	2	1	607	75%
0·25 mega unit for 20 days	8	3	1	1	3	634	25%
0·25 mega unit for 28 days	10		1	3	6	544	40%
0·5 mega unit for 28 days ..	10	3	2		5	465	20%
Total	35	6	5	7	17		34%
Expected numbers from Tables I, II, and III		11·7	0·9	6·6	15·8		21%

organism to penicillin has been acquired; but that is probably seldom an important factor, since in 50 patients that relapsed and were treated again an increase in resistance was observed only in 12—in five the increase was less than threefold, and in seven it was more than threefold—and in three the resistance decreased. Another possibility is that these patients belong to a selected group of those who are naturally resistant to treatment. The nature of this resistance is not known, but it is conceivable that in some individuals the infecting organisms are so buried in avascular tissue that the drug does not reach them in lethal concentration. Whatever may be the cause, it is clear that patients who have relapsed should be given a more generous system of dosage. A course of 2 million units a day for eight weeks is suggested, but it is possible that even larger doses should be given.

Relapses seldom occur more than a month after treatment (Table VI), but a long period of follow-up shows that

TABLE VI.—*Relapses after Treatment*

Interval between Treatment and Relapse	Relapse after Treatment Lasting 20 Days or More	Relapse after Treatment Lasting 10 Days or Less
0–10 days	20	19
11–20 „	14	3
21–30 „	7	4
31–40 „	—	1
41–50 „	3	—
51–60 „	2	1
Over 60 „	3*	1†

* Relapsed after 130, 250, and 390 days.
† Reinfected with different organisms after 161 days.

a small risk remains even after a year or more of good health. Whether these delayed relapses are due to reinfection or are an indication of dormant infection in the heart valves is uncertain.

The Infecting Organism

In 245 patients the infecting organism was a *Streptococcus viridans*, in 17 a non-haemolytic streptococcus, in 3 a staphylococcus, in 2 a micro-aerophilic streptococcus, in one *Haemophilus influenzae*, and in one the organism was not identified. Patients from whom a positive blood culture was not obtained were excluded from this series. The relationship of the sensitivity of the infecting organisms to the results of treatment is most interesting (Table VII).

TABLE VII.—*Comparison of the Results of Treatment with the Sensitivity of the Organism to Penicillin. (Resistance expressed as a multiple of the resistance of the standard Oxford staphylococcus.) None of the Patients had Previously been Given a Long Course of Treatment*

Dose		Coefficient of Resistance: 1 or Less	2	3–6	8–16	32 or More	Not Known	Total
0·1 mega unit a day for 28 days	Died controlled	3	1					
	Died uncontrolled					1		
	Relapsed ..	7	1				1	
	"Cured" ..	6	1					
0.25 mega unit a day for 20 days	Died controlled	5	1	2			1	
	Died uncontrolled				1			
	Relapsed ..	5						
	"Cured" ..	6	2	1			2	
0.25 mega unit a day for 28 days	Died controlled	17	7	3			3	
	Died uncontrolled	1		2				
	Relapsed ..	11	1	1			1	
	"Cured" ..	28	10	4	1		3	
0·5 mega unit a day for 20 days	Died controlled		1		1			
	Died uncontrolled							
	Relapsed ..		1	1				
	"Cured" ..	4	2	1		1		
0.5 mega unit a day for 28 days	Died controlled	11	6	2	1		5	
	Died uncontrolled		2	1	1	1		
	Relapsed ..		1					
	"Cured" ..	23	7	3	2	1	1	
All doses	Died controlled	36	16	7	2	—	9	70
	Died uncontrolled	1	2	3	2	2	—	10
	Relapsed ..	23	4	2	—	—	2	31
	"Cured" ..	67	22	9	3	2	6	109
Total		127	44	21	7	4	17	220
Relapsed or died infected ..		19%	13·6%	24%	28%	50%	12·1%	18·7%

The percentage of patients who relapsed or died uncontrolled did not appear to be affected by the resistance of the organism over a considerable range. However, our experience during the past year and that of others suggests that when the coefficient of resistance is more than about 8, daily doses larger than 500,000 units should be given, probably over a period longer than 28 days. The system of dosage adopted must depend on the resistance of the organism, and recently we have used as much as 40 million units a day. Fortunately the incidence of organisms more than eight times as resistant as the Oxford staphylococcus is low. The majority were as sensitive to penicillin as the Oxford staphylococcus, sometimes more sensitive; and Table VII clearly shows that even this degree of sensitivity is no indication for a reduction in dosage.

Foci of Infection.—It is generally accepted that every effort should be made to remove foci of infection, particularly in the teeth, and this should be done while the patients are receiving penicillin. There is no proof in this series of the efficacy of this procedure, but so long as any uncertainty exists as to the likelihood of reinfection it seems reasonable to assume that foci of infection should be eradicated.

Causes of Death

In this series 131 patients, or 49%, have died, but many of these received what would now be considered inadequate treatment. Of those whose infection was apparently controlled about 35% have subsequently died of various complications. The majority of deaths occurred either during treatment or soon after treatment was completed (Table VIII). Heart failure caused 40% of the deaths, and was a major cause in another 16% (Table IX). Comparatively few died of uraemia, emboli, or haemorrhage, and in 19% the cause of death was mixed or uncertain. The

TABLE VIII.—*Interval between Treatment and Death*

	Died with Infection Apparently Controlled	Died with Infection Not Controlled	Total
Died during treatment ..	29	8	37
" 0– 49 days after ..	32	19	51
" 50– 99 " " ..	15	4	19
" 100–149 " " ..	8	3	11
" 150–199 " " ..	1	2	3
" 200–249 " " ..	3	1	4
" 250–500 " " ..	6	0	6

TABLE IX.—*Cause of Death*

	Died During Treatment	Died After Treatment	Percentage of Total Deaths
Heart failure	7	45	40
Heart failure and other causes	7	14	16
Uraemia	3	5	6
Emboli	6	9	11
Haemorrhage	4	6	8
Mixed or uncertain	10	15	19
Total	37	94	100

remarkably high death rate from heart failure is of considerable interest and will be referred to later.

The heart valves were examined at necropsy in 47 cases. In 39 of these infection had apparently been controlled by penicillin, and yet what appeared to be living organisms were seen in the heart valves of 13; organisms of uncertain viability were seen in 4; and organisms which appeared to be dead in 9. In the remaining 8 patients infection was not clinically controlled; in 6 of these, apparently living organisms were seen in the heart valves, and in 2 no organisms could be demonstrated. It would be unwise to draw definite conclusions from these results until further evidence of the viability of the organisms is forthcoming. Nevertheless it is disconcerting, to say the least, to find apparently living organisms in the heart valves of one-third of patients in whom, according to the usual clinical criteria, infection had been controlled.

Factors in Prognosis

Death from heart failure and other complications is now a much greater hazard to the patient than the risk of failure to respond to penicillin, and it is therefore of clinical importance as well as of academic interest to estimate this hazard when treatment is started. Tables X–XIII show the significance of certain clinical observations made before treatment began.

The nature of the primary cardiac lesion (Table X) appeared to be of slight significance; the highest death rate was found in combined mitral and aortic lesions (59%), and the lowest in septal defects (33%). Four patients had a patent ductus arteriosus; three of these recovered and one died with the infection uncontrolled. There were 5 patients with mitral stenosis and auricular fibrillation, and one of these died.

TABLE X.—*Relation of Primary Cardiac Lesion to Prognosis*

Primary Cardiac Lesion		Total No.	"Cured"	Died	
				No.	%
Rheumatic	Mitral	120	69	51	43·0
	Aortic	29*	15	14	48·5
	Mitral and aortic ..	90	37	53	59·0
	Unspecified	1	1	—	—
	Total	240	122	118	49·0
Congenital	Septal defect	12	8	4	33·0
	Others	17	8	9†	53·0
	Total	29	16	13	45·0

* Including 10 patients in whom a rheumatic history was not given: 5 of these died.
† Including 5 patients with bicuspid aortic valves.

Evidence of heart failure (Table XI) is of considerable importance. Of those with no evidence of heart failure 36.4% died, and of those with moderate heart failure 75% died. The 28 patients who had severe heart failure when treatment was started all died.

TABLE XI.—*Relation of Heart Failure to Prognosis*

Degree of Heart Failure Before Treatment	Total No.	"Cured"	Died				Deaths (%)
			During Treatment	Within 50 days	Within 100 days	After 100 days	
None	201	128	20	23	9	21	36
Moderate ..	40	10	8	16	6	—	75
Severe	28	0	9	12	4	3	100
Total ..	269	138	37	51	19	24	49

The duration of infection (Table XII) is also significant: of those recently infected 34% died, while of those infected for six months or more over 60% died.

TABLE XII.—*Relation of Duration of Infection to Prognosis*

Duration of Infection	Total	"Cured"	Died	
			No.	%
0– 9 weeks	94	62	32	34
10–19 "	91	45	46	51
20–29 "	59	22	37	63
30–39 "	13	4	9	69
Over 40 "	12	5	7	58
Total	269	138	131	49

The state of nutrition of the patient (Table XIII) was of surprising importance. The questionary filled in before treatment was started gave a choice of four categories. Of those in a "good" state of nutrition 30% died; when nutrition was "poor" 55% died; when it was "bad" 65% died; and only 2 out of 16 "emaciated" patients recovered—a mortality rate of 87.5%. The significance of nutrition when analysed appears to be independent of the duration of infection or of the incidence of heart failure. For instance, there were 201 patients without evidence of heart failure: in 90 of them nutrition was good and 26% died, in 101 nutrition was poor or bad and 41% died, and of 10 who were emaciated 80% died. These results emphasize the need for an adequate calorie intake as with other prolonged fevers.

TABLE XIII.—*Relation of the State of Nutrition to Prognosis*

State of Nutrition	Total No.	"Cured"	Died During Treatment	Died After Treatment	Total Died	
					No.	%
Good	102	71	11	20	31	30
Poor	125	56	14	55	69	55
Bad	26	9	8	9	17	65
Emaciated ..	16	2	4	10	14	87·5
Totals ..	269	138	37	94	131	49

The ages of these patients ranged from 7 to 67, with a mean of 31 years (S.D. ± 11.9). Age was of doubtful prognostic significance except in the group over 50. In those under 50 the death rate was 46%, and in 26 patients over 50 it was 69%.

Discussion

It is not within the scope of this report to review the literature on the treatment of subacute bacterial endocarditis, and the emphasis on our own results is not due to any lack of appreciation of the pioneer work in America on the use of penicillin in this disease. Our own series is the largest yet published, and our conclusions regarding treatment are in accord with those of most who have worked in this field.

Although penicillin can now be expected to control the infection in about 90% of patients, a closer inspection of our results shows several features which are far from satisfactory and which reveal our ignorance of several important aspects of this disease : (*a*) In the majority of patients who relapse no good reason can be given for the failure of penicillin ; in only a few could it be explained on the basis of a highly resistant organism. (*b*) The remarkably high incidence of heart failure, both during and soon after apparently effective treatment, is not explained. (*c*) The presence in the heart valves of what appeared to be living organisms in about one-third of patients who died after apparently effective treatment suggests that dormant infection may be an important sequel of treatment with penicillin.

For these and other reasons we believe that further intensive research on this disease is indicated, with particular emphasis on higher dosage and on careful analysis of post-mortem material. The following centres are continuing this work, and it is hoped that an adequate number of patients will be referred to them: Belfast (Queen's University, Institute of Pathology). Birmingham (Professor Wilkinson, Queen Elizabeth Hospital). Bristol (Professor Bruce Perry, Bristol Royal Infirmary). Edinburgh (Dr. A. R. Gilchrist, Royal Infirmary). London (Sir Alexander Fleming, St. Mary's Hospital ; Professor Christie, St. Bartholomew's Hospital ; Dr. G. E. S. Ward, Middlesex Hospital). Manchester (Professor Crighton Bramwell, Royal Infirmary). Leeds (General Infirmary).

Conclusions

The administration of 500,000 units of penicillin a day for 28 days can be expected to control the infection in about 90% of patients suffering from subacute bacterial endocarditis, but about 35% of these die of heart failure and other complications.

Larger doses should be given for a longer period of time to patients who relapse and to patients in whom the infecting organism is more than eight times as resistant as the Oxford staphylococcus.

Of the relapses 90% occurred within a month of treatment, but a danger of relapse persists after a year or more of good health.

Evidence of heart failure or of poor nutrition is of great importance in prognosis. The duration of infection and the nature of the primary cardiac lesion are also of some significance.

What appear to be viable organisms are not infrequently found in the heart valves of those who have died after the infection has apparently been controlled.

This report is made on behalf of a large number of clinicians and bacteriologists who have taken part in this investigation. Dr. J. E. Cates and Dr. P. J. N. Cox have also assisted in the analysis of results. Mr. J. A. Heady and Professor Bradford Hill have given valuable help and advice on statistical analysis.

One of the special duties of the local health department is to disinfest verminous properties and persons. *Insect Pests*, by W. C. Harvey and H. Hill (2nd ed., pp. 347, 14s.; H. K. Lewis and Co., London, 1947), is a useful handbook for the medical officer or sanitary inspector, particularly for its account of practical procedure and legislative control. The biological data about the various pests form the weakest section of the book; there are also some errors and misspelt specific names. The quality of the illustrations varies: about half are photographs which, for such difficult subjects, are fairly good; the rest are drawings and are rather poor. The authors have enlarged this edition to include information about mosquitoes and moths (clothes moths), which for some mysterious reason they discuss in the same chapter. There is an informative chapter on the new insecticides, such as D.D.T., and the authors have taken pains to describe the practical applications of these materials.

INTRAVENOUS ALIMENTATION*

BY

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The proper functioning of the body in all or any of its parts demands a sufficiency of all essential nutrients. I mention this obvious fact merely for emphasis. When injury or disease of an incapacitating degree occurs nutrition is nearly always interfered with and malnutrition may be said to have begun. The two main causes are: (*a*) the direct effect of the disease or injury leading to destruction of tissues and loss of nitrogen, and (*b*) inability (or disinclination) to take and retain food. If destruction of tissue continues unchecked malnutrition becomes progressive and a vicious circle begins ; the disease causes digestive upsets or anorexia, or both, which in turn aggravate the disease. The clinician then has on his hands the original diseased state complicated by starvation or semi-starvation. He will attempt to break the vicious circle by removing the cause of the tissue destruction or by checking it, and he will probably try to supply nutrients to the tissues so as to combat the malnutrition and assist the body to overcome the primary condition. In chronic conditions, too, these considerations are relevant, and superadded infections, bed sores, or hypostatic pneumonia may develop and make further contribution to the vicious circle.

By malnutrition I mean derangement of the physiological processes concerned in the supply of essential nutrients in sufficient amounts to any and every part of the body and with their metabolism. Although it includes in the broad sense the effects of excess of some or all nutrients, such considerations are not germane to this paper, and I therefore restrict the meaning of the term to the effects of failure of all nutrients or of some to reach the tissues in sufficient quantities. Malnutrition in this sense might be caused by inability to swallow food—e.g., in stenosis of the oesophagus and comatose states: by inability to retain and digest food—e.g., in cyclic vomiting ; by failure of absorption—e.g., in persistent diarrhoea. In infective states of long duration, happily less common now than before the introduction of the sulphonamide drugs and penicillin, malnutrition is a prominent feature, partly because of anorexia and partly because of impaired digestion and assimilation ; and if stupor and the "typhoid state" supervene inanition becomes absolute and a fatal issue is a matter of time. If the clinician were able to supply nutrients to the body, not merely to stave off starvation but also to supply the elements to reconstruct the damaged tissues and to form antibodies, the outlook would at once be transformed.

Thanks to researches in recent years, we are now able by means of intravenous alimentation to meet such situations with much greater confidence than formerly. Hydrolysates of protein suitable for intravenous use were first prepared about seven or eight years ago. Before that time intravenous alimentation was confined to the use of saline and glucose solutions, the value of which is strictly limited because of the absence of protein.

Protein Requirements

In the conditions we have been considering it is protein that is specially required.

Metabolizable Proteins.—The intestinal villi cannot absorb proteins until they have been hydrolysed by digestion

* Substance of a lecture given to the North of England Branch of the British Medical Association on May 8, 1947.

to amino-acids and peptides. The body is intolerant of foreign proteins, and if they get into the blood they cause reactions of an anaphylactic type. Human blood proteins can, however, be given by vein with impunity, and there is evidence, provided mainly by Madden and Whipple (1940), that blood proteins can supply the "building stones" required for the construction of the body's tissues. For long it was assumed that the amino-acids, after being absorbed, went via the portal vein to the liver, where those not wanted by the body were de-aminized and the non-nitrogenous residue used for energy, while those required for growth or repair by any organ or tissue were taken up from the general circulation. Whipple, on the basis of much experimental evidence, has advanced an attractive theory about the fate of absorbed amino-acids (and peptides). It is that (*a*) the amino-acids are changed, mainly in the liver, into plasma proteins; (*b*) there is a constant ebb and flow between plasma and tissue proteins; (*c*) in the tissues there is a reserve store of protein for emergency use; and (*d*) normally a state of dynamic equilibrium exists between the plasma proteins, the reserve proteins, and those ingested.

Blood Proteins.—It would follow from Whipple's theory that we have had, since blood transfusion became perfected, a means of supplying by vein all the proteins the body requires; but it is doubtful if supplies of human blood available, or likely to be available in the near future, would suffice for the very many uses to which human plasma could be put in intravenous alimentation. Moreover, we do not know whether plasma proteins can be used for energy purposes. As I point out later, a large proportion of the energy needs of the patient treated by intravenous alimentation must, in the present state of knowledge, come from the proteins injected. The use of plasma is therefore likely to be confined to the purposes for which it was originally intended—namely, to combat shock and the effects of haemorrhage and of certain diseases.

Protein Hydrolysates.—Loewi in 1902 was evidently the first to show that nitrogen equilibrium and weight could be maintained by administering protein digests by mouth. He fed dogs on pancreatic digests of protein, plus starch and fat. In 1913 Henriques and Andersen kept goats in N and weight equilibrium for twenty days with intravenous protein digests, sugar, and salts. In 1938 Rose showed that ten of the thirty or so known amino-acids, given by mouth as the only source of N, sufficed for maintenance of N balance and weight in rats. The practical significance of these findings did not become apparent until Elman and Weiner (1939) reported the successful administration of protein digests by vein to human patients. Since then increasing attention has been given to the subject, and there are at present on the market American and British hydrolysates of proteins, which can be given to human patients day after day in substantial quantities without reaction and often with striking success. The subject has been reviewed by Elman (1944), Cuthbertson (1944), and Gaunt (1944).

Hydrolysis of protein can be effected by acids or by enzymes, but enzymic preparations have been found to be the more successful. The earlier preparations often provoked reactions which were caused, as animal experiments showed, either by toxic substances produced by bacteria or by large polypeptide aggregates. The enzymic preparations now used very extensively in North America seem to be practically free from such risks and less prone than acid digests to cause thrombosis. An enzymic preparation made in this country, and at present being submitted to extensive trial under M.R.C. auspices, appears also to be giving satisfactory results, but further experience must be gained before its full therapeutic value can be stated.

Amino-Acids

Madden and Whipple (1946) have done much experimental work on dogs to ascertain whether solutions of pure amino-acids given parenterally could maintain the animals in N equilibrium. The work of Rose (1938), showing that only ten amino-acids are essential, simplified the trials of Whipple's school. He was able to secure substantial quantities of these amino-acids, most of them synthetically prepared, and showed that, when given by mouth, skin, vein, or peritoneum along with glucose, they sufficed for N equilibrium, but weight was not wholly maintained. Whipple, when I saw him in his laboratory in October, 1946, expressed the opinion that another protein element, perhaps a peptide, is essential for health, and it may well be the strepogenin of Woolley (1946); I will take this up later.

All synthesized amino-acids are in racemic form—i.e., a mixture of the natural and unnatural isomers. The animal body can make use of only the natural isomers, and the unnatural forms, which Madden and Whipple (1946) and Madden *et al.* (1946) found to be non-toxic to man, however administered, are excreted unchanged by the urine. The ten essential amino-acids are: threonine, valine, leucine, isoleucine, lysine, tryptophan, phenylalanine, methionine, histidine, and arginine. The use of mixtures of these on an extensive scale is out of the question; they are difficult and very costly to manufacture.

Rose *et al.* (1942, 1943), who maintained young men for several weeks on a diet of which the N was in the form of amino-acids, are of the opinion that arginine and histidine are less essential for man than for the other animals tested. Madden, Whipple, *et al.* (1945) have always incorporated glycine in the amino-acid mixture given to human patients because this seems to make it better tolerated. They have reported the maintenance of, and even gains in, weight of several patients suffering from various diseases with mixtures of the ten essentials and glycine given by vein, skin, or mouth, plus small amounts (about 7 g.) of protein by mouth. It may well be that the protein consumed by mouth filled the part of strepogenin in the animal experiments. One patient suffering from ulcerative colitis was kept going in this way for 100 days, during which a gain in weight of 11 kg. occurred (Madden *et al.*, 1946).

Strepogenin.—Woolley (1946) found that a peptide which he isolated from certain crystalline proteins, including insulin, and which is essential for the growth of haemolytic streptococci, is necessary also for the growth of mice in addition to the ten essential amino-acids plus glycine. He called the peptide "strepogenin." Strepogenin is present in enzymic hydrolysates but not in acid ones.

Urinary Leakage after Injections

Whipple and his colleagues found that, soon after giving amino-acids intravenously, substantial amounts were rapidly excreted in the urine; the excretion was less when they were given by the skin and least by mouth. Clinicians here and in America have found that large amounts of N are lost in the urine in the first half-hour or so after giving hydrolysates by vein. The losses can be detected even by the appearance and smell of the urine. This raises the important question whether, in normal absorption from the intestine, amino-acids undergo any change in physical or chemical properties in passing through the intestinal wall and the liver. It may be that the epithelium

renders the amino-acids more easily metabolized or convertible into plasma proteins. Kotschneff (1926) claims to have found in dogs an increase in polypeptides in the portal vein during absorption of protein meals and of amino-acids. The findings of Madden and Whipple (1946), showing that amino-acids given orally result in better production of blood proteins than when given by vein, support Kotschneff. He used the technique of London (1927), which enables blood to be drawn from the deep blood vessels in unanaesthetized animals. Analysis of blood samples from the portal and hepatic veins of dogs before and after protein meals by modern biochemical methods would be worth while.

There is an important difference between the routes followed by amino-acids absorbed in the ordinary way and by intravenously injected amino-acids or hydrolysates. Normally, of course, all the amino-acids pass via the portal vein to the liver, and, as we have seen, the great bulk of them are apparently changed into polypeptides and proteins. Small amounts of amino-acids are, however, found in the general circulation, but evidently not in such high concentrations as after injections of amino-acids or protein digests. The injected hydrolysates go in the venous blood to the right heart, the lungs, the left heart, and thence in the arterial blood all over the body. If, according to the older theory, the amino-acids were straightway used by the tissues of the body, leakage by the kidney would probably not be as great as it is, but if they must first be changed into blood proteins by the liver, according to Whipple's view, then the dispersal of the material through the circulation would make the necessary transformation in the liver and removal of amino-acids from the blood a very gradual process. The kidney threshold for the separate amino-acids may thus be exceeded. This, it seems to me, is the main reason for the losses of N by the kidney after intravenous infusions. There are clearly many gaps in our knowledge, and it is important that steps should be taken to fill them.

Clinical Experiences

Notwithstanding our lack of knowledge, there is no doubt that protein hydrolysates have provided much success, even where their use has been very limited, as in this country. Very few cases have, however, been published. Two interesting ones came under my observation (Magee, 1946). Both were cases of homologous serum jaundice and were *in extremis* before treatment began; the response and recovery were spectacular. They were given 5% acid hydrolysate in amounts up to 1,000 ml. in twenty-four hours (50 g. of protein and 200 calories) at the rate of 500 ml. in about three hours. The hydrolysates were usually preceded and sometimes followed by 500 ml. of 5% glucose given in amounts up to 1,600 ml. (320 calories) in 24 hours. The rate of administration in North America varies from 350 to 600 ml. an hour of a 5% solution each of digest and glucose, and about 4 litres is apparently the maximum that can be given with impunity in twenty-four hours (200 g. of protein and 1,600 calories). Experience there indicates that it would be difficult to exceed this amount because of the care and attention required for the infusions and because of the risk of reactions and extensive thrombosis.

The conditions in which protein hydrolysates have been used with success include hepatitis, injury or disease of the bowel, intestinal obstruction, severe typhoid state, enteritis, colitis, severe burns, cyclic vomiting, peptic ulcers, and after operations. The most striking case I know of was reported by Brunschwig *et al.* (1945). The patient was kept alive for eight weeks entirely by venous infusions of protein hydrolysate plus glucose, and during this time he had two severe operations—one for removal of a tumour and the other a bowel resection. Brunschwig, when I saw him in October, 1946, informed me that the man was enjoying a normal life about two years after his discharge from hospital.

Thrombosis

Thrombosis has occurred in every case treated with acid preparations that I know of in this country, but it would seem that it is less likely to occur with enzymic preparations. Although they have rarely reported thrombosis in their papers I found that the Americans have also been bothered with it. Brunschwig told me that in his famous case so many superficial veins were affected that he had difficulty in giving injections towards the end of the treatment. The Americans are now combating this complication with fair success by using different veins and giving no more than 500 ml. at a time by the same vein. Joliffe showed me in a New York hospital a novel method of infusion in an emaciated patient—through a cannula tied into a vein. He treated this patient with blood, then protein hydrolysate for a week, and later with a 25% solution of albumin. The improvement in the patient was remarkable. She had had a large intestinal resection and was in desperate plight before the treatment was started.

Energy Requirements

The energy requirement of an adult male confined to bed is probably not much less than 2,000 calories daily, and may be 2,400 or more in febrile states. If the maximum we can give by vein is substantially less than this, then we run the risk of the hydrolysates being used largely for energy purposes, so that nothing would be left over for reconstruction of damaged tissues. It is to avoid this that glucose is given immediately before or in solution with hydrolysates. To what extent this succeeds is unknown, but the question would not arise if we were able completely to satisfy the energy needs from non-protein sources and have, say, 70 g. of protein for reconstruction. This cannot be done with any combination of hydrolysates and glucose because stronger solutions are excluded owing to the risk of extensive thrombosis and losses via the kidneys, and with solutions of the present strengths the bulk of fluid which would have to be given would be too great.

Fats

As we have seen, the maximum energy we can hope to give by vein day after day is only 1,600—i.e., 400–800 calories less than requirements. There can be little doubt, therefore, that a large proportion, maybe all in many cases, of the injected hydrolysate is oxidized for energy, thus frustrating its primary purpose—namely, tissue reconstruction. Now that we have succeeded in making digests of proved value on a commercial scale, the problem remaining to be solved is how to "protect" the protein hydrolysates by sufficient non-protein energy-giving materials so that the bulk of the amino-acids and peptides will be spared for tissue-building. To do this we would require to give 2,000 calories or more a day in non-protein form.

At present we have no means of giving fats and are therefore restricted to glucose, but the maximum energy we can provide in this form is only about 800 calories a day. The energy problem then becomes one of incorporating fat in usable form in the injections. If this were possible we could reduce the protein hydrolysate to about 75 g. more or less—i.e., to 1,500 ml. of a 5% solution. It would, however, be better to increase the fluid to 2,000 ml. and reduce the concentration of digest to 3.5%, thereby lessening the risk of leakage by the kidney.

With glucose in a concentration of 5% this would give 400 non-protein calories, leaving 1,600 to come from fat in order to reach the 2,000 target. About 170 g. of fat would be required.

So far it has not been found possible to give to human subjects fats in amounts that matter, but research is proceeding. Hegsted, Hay, and Stare (1945) have got so far as to risk giving small amounts to patients, but reactions, none serious, have followed in several instances. Dunham and Brunschwig (1944) have also busied themselves on the subject, experimenting with dogs, but apparently with little success. The main difficulty seems to be to get an emulsion stable enough to stand sterilization. Ivy has been working vigorously on the subject, and he informed me at the International Physiological Congress in Oxford in July, 1947, that he had succeeded in making a stable emulsion with which he has kept dogs in N balance, constant weight, and good health by exclusively venous feeding for 42 days. Since then he has been good enough to send me the following particulars of his emulsion.

Preparation of the Emulsion

1. 50 g. of butter oil refined.
2. 2 g. of lecithin "purified."
3. 2.5 g. of "span 20" (a wetting agent).

Mix thoroughly and heat and mix on a steam bath. Then add, stirring, to :

4. 445 ml. of either 5% or 10% glucose solution made in triple-distilled water and containing 0.1% sodium cholate.

Homogenize five times at a pressure of 3,000–4,000 lb. per square in. (210–280 kg. per cm.^{2}) in a Cherry-Burrell viscolizer (junior model) or its equivalent. Autoclave twice at 10 lb. for 10 minutes within 24 hours.

This yields a mixture of : 10% fat by weight, 0.4% lecithin, 0.5% span 20, 0.1% sodium cholate, 5% glucose.

1. The butter oil is refined by melting and removing curd and water. Then the oil is washed with three or four volumes of hot freshly distilled water three times. Highly refined oil may also be used, though most experiments have been done with butter oil.

2. The "purified lecithin" is a soya-bean lecithin prepared by the "Lecithin" Products Co., Elmhurst, New Jersey. If the lecithin is not purified, or even if a 1% concentration of this lecithin is used, anaemia results.

3. Span 20 is a sorbitan wetting agent made by the Atlas Powder Company, Wilmington, Delaware. It is the best (non-toxic) of numerous wetting agents so far used.

4. Sodium cholate is obtained from Breon and Co., of Kansas City, Missouri, or G. D. Searle and Co., of Chicago.

The emulsion is infused slowly intravenously so that the total calorie and nitrogen requirement is given in six to eight hours. Various protein hydrolysates have been used (one by Mead Johnson and Co., Evansville, Indiana, and another prepared by Cutter Laboratories, Berkeley, California). Enough of the hydrolysate is given to keep the dogs in N balance. It can be used separately or mixed with the emulsion.

The total daily mineral and vitamin requirement may be added to the solution. Calcium and iron may disturb the emulsion ; these should be given separately.

There can be no doubt that if we succeed in making a preparation suitable for human intravenous use and containing about 75 g. of protein hydrolysate and 2,000 non-protein calories in 2 litres or so we shall have a therapeutic agent of great possibilities. This work of Ivy and his colleagues is an important step in that direction.

Summary

Until recent years we had no adequate means of combating the malnutrition which complicates many diseases, especially those directly hindering the ingestion, digestion, absorption, or metabolism of food. A preparation of protein suitable for intravenous use and metabolizable by the body was required. Although there is evidence suggesting that the plasma proteins can supply the elements for tissue growth and repair, it is doubtful if transfusion with human plasma is the solution of the problem ; sufficient human blood might not be obtainable for such extensive use.

Enzymic hydrolysates of protein suitable for administration by vein have been prepared in U.S.A. and Great Britain and have been used with impunity and success in a wide variety of conditions in which secondary malnutrition is a prominent feature. They include acute hepatitis, comatose states, typhoid state, infantile diarrhoea, and post-operative conditions. The hydrolysates are usually given in 5% solution with 5% glucose at about 500 ml. an hour to a maximum of about 4 litres (200 g. of protein and 1,600 calories) in twenty-four hours. Thrombosis can be lessened by using different veins and giving no more than 500 ml. at a time by the same one.

A defect in the present procedure is that a large proportion of the injected hydrolysate is oxidized to supply energy and is thus diverted from its intended purpose of tissue-building, because it is not yet possible to incorporate enough non-protein calories in the infusion fluid.

It is desirable to administer up to 2,000 calories as glucose and fat emulsion ; the hydrolysate could then be reduced to about 2,000 ml. of a 3.5% solution (70 g. of protein) and the bulk would probably be used for tissue repair.

It has not yet been possible to make a fat emulsion suitable for human use ; but dogs have been kept in N equilibrium for six weeks by intravenous feeding on protein hydrolysates and glucose–fat emulsions which withstand sterilization.

An important problem remaining to be solved is to check the urinary leakage of hydrolysate which occurs in the first thirty minutes or so after starting infusions.

I am indebted to Prof. Himsworth and Dr. Stannus for comments on the paper, and especially to Prof. Ivy for his great courtesy in allowing me to publish for the first time the details of his fat emulsion.

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The number of technical dictionaries available to the medical worker interested in foreign languages is very limited, and any reliable addition to their number is welcome. The *English–Spanish Chemical and Medical Dictionary*, by Morris Goldberg (pp. 692, 50s. ; McGraw-Hill, New York, 1947), will be of more use to Spanish-speaking medical men than to their English-speaking colleagues and should provide them with a fairly complete guide to British and American technical terms. The dictionary is up to date and includes such newcomers to medicine as streptomycin and thiouracil. Definitions of words are given in Spanish. It is inevitable that in a new book there should be a number of relatively important omissions. For example, the author has omitted the names of some muscles while including others less commonly referred to. Nevertheless, he has prepared the dictionary as a whole with care, and we can recommend it not only to those interested in medicine and the allied sciences but also to chemists and biologists.

RARER MANIFESTATIONS OF HERPES ZOSTER

A REPORT ON THREE CASES

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Herpes zoster usually presents as a mild illness with a characteristic rash accompanied by local pain and preceded by a varying degree of constitutional disturbance. Post-herpetic neuralgia is a common sequel, but complications are rare. Of the complications which have been recorded a concomitant varicelliform eruption is perhaps the most common. The rarer, and more serious, complications include lesions of the motor neurones, myelitis and meningitis, encephalitis, and osteoarthritis (Wilson, 1940). It is the occurrence of such complications that at once dispels the concept of zoster as a uniformly benign infection confined to the sensory neurones. Moreover, these complications open controversial aspects on the aetiology and pathology of the disease and upon the difficult problem of the relationship between zoster and varicella. The following three cases are placed on record as exemplifying certain of these rare complications. All three patients showed evidence of affection of motor neurones, and two of them exhibited a generalized eruption during the course of the disease.

Case 1

Zoster, accompanied by paralysis, in the distribution of the fifth cervical segment.

A solicitor's clerk aged 60 was admitted to hospital on July 4, 1947. He gave a history of chicken-pox in childhood. In 1918 he had sustained a shrapnel wound of the right elbow, which had left him with a complete ulnar lesion on that side and much limitation of movement of the elbow-joint.

Six weeks before his admission he had suffered from acute pain in the right shoulder. Three days later a rash appeared in the antecubital fossa and rapidly spread up the outer side of the arm as far as the right shoulder. Three days after the appearance of the rash he noticed, quite suddenly, that his right arm was weak and that he could raise the arm from the side only with difficulty. The weakness increased over the next few days until the right arm was quite useless. Since that time the rash had cleared up, but the weakness had not improved at all. After the disappearance of the rash he had felt tingling and numbness in the area of skin previously affected.

Examination showed a healthy well-built man. There was a pigmented scarring over the site of the recent rash, distributed on the outer side of the upper arm from the shoulder to the elbow—i.e., in the cutaneous distribution of the fifth cervical dermatome. There was some hypo-aesthesia to pin-prick and cotton-wool sensation in the same area. There was considerable wasting of the right deltoid, supraspinatus, and infraspinatus muscles. No abduction of the shoulder was possible, although a flicker of muscular contraction was palpable over the deltoid muscle when abduction was attempted. Slight contraction of the supraspinatus and infraspinatus was likewise palpable over the muscle bellies. The biceps and brachioradialis muscles on the right side were weaker than those on the left. Under the nomenclature suggested by the Medical Research Council (1942) the muscular contractions at this time were : deltoid 1, supraspinatus 1, infraspinatus 1, biceps 4, brachioradialis 4. There was a deep scar of the old wound on the inner side of the right elbow, and below the elbow there was a complete ulnar-nerve palsy. The biceps and supinator reflexes on the right side were impaired; the triceps-jerk was normal. The remainder of the physical examination revealed nothing abnormal. Lumbar puncture on July 6 showed a clear fluid under normal pressure. The cerebrospinal fluid contained 5 cells per c.mm. The protein was 0.055% with a slight increase of globulin, and the chlorides 0.75%. The Wassermann reaction and Lange curve were negative.

The patient was treated by resting the arm in an abduction splint and by faradic stimulation of the muscles affected. He was discharged from hospital on July 30 to continue treatment as an out-patient, and at this time there was pronounced objective improvement. He was last seen on Aug. 16, when recovery was almost complete.

Case 2

Ophthalmic zoster with generalized eruption, followed by weakness of the levator palpebrae.

A housewife aged 48 was admitted to hospital on July 9, 1946. There was no history of previous illness, and she denied having had chicken-pox. She complained of an irritation on the left side of the forehead for the previous week, and on July 6 she had first had severe neuralgic pains over the left eyebrow. On the day before admission the left eye became swollen and painful, and a rash was noticed on the forehead. On admission the patient looked ill and had a fever of 101.8° F. (38.8° C.). There were a moderate number of vesicles on erythematous bases in the distribution of the ophthalmic division of the trigeminal nerve on the left side. The left eye showed conjunctival injection, with some photophobia and extreme tenderness to pressure. There were no other abnormal signs, and the rest of the skin was clear. During the next three days (July 10 to 12) the number of vesicles increased, the erythema spread, and the upper and lower lids became grossly oedematous. The appearance was now quite typical of a severe herpes zoster.

On July 13 the patient complained of irritation of the skin. Examination then showed that she had a generalized eruption on the trunk and proximal parts of the limbs, with a single lesion on the face. The eruption was quite typical of that seen in varicella, and the subsequent course of pustule formation and healing followed as customary in that disease. It was noted, however, that after the first 24 hours no fresh crops of vesicles arose. Whether or not the previous lesions had occurred in crops is not known, as no examination of the skin had been carried out between the initial examination and the complaint of irritation. As the herpes recovered it was evident that there was considerable weakness of the levator palpebrae muscle on the left, giving rise to obvious ptosis. The scabs from the varicelliform rash separated on Aug. 1, 14 days after their occurrence, and the patient was allowed to leave hospital. The ptosis was still present on discharge and persisted for many weeks. The patient was last seen in December, 1946, when the ptosis had completely recovered. At no time was there any oculomotor paralysis or abnormality in the pupil response.

Case 3

Zoster of trigeminal and cervical distribution accompanied by generalized eruption and followed by facial palsy.

An engineer aged 43 was admitted to hospital on July 13, 1947. In his youth he had suffered from scarlet fever, diphtheria, and chicken-pox. In February, 1945, he developed shingles over the lower half of the left side of the face, the upper part of the neck, and behind the left ear. He stated that in spite of careful search no lesions were found in the ear or inside the mouth. Four days after the appearance of the zoster he developed "an attack of chicken-pox," and because of this he was transferred to an isolation hospital. Within a day or two he suddenly developed a complete left facial palsy, which persisted until his discharge from hospital some five weeks later. Since that time there had been some improvement in the weakness of the face, but he had always been greatly troubled by difficulty in eating, numbness of the face, and severe neuralgia. His present admission followed a cerebral vascular accident which had occurred twelve weeks previously and which had caused aphasia and weakness of the right arm and face. The disability arising from this cerebral lesion had almost disappeared on admission.

Examination showed a pronounced left lower neurone facial weakness, together with diminished sensations over the lower

part of the face and on the inside of the left cheek. The tongue was protruded centrally. Although the patient complained of lack of appreciation of taste on the left side of the tongue, the presence of hemiageusia was not confirmed by crude tests. In addition to these signs there was an increase in the tendon reflexes and a diminution of the abdominal reflexes on the right, representing the residuum of the recent cerebral thrombosis. His blood pressure was 210/120. No other abnormal findings were present. Lumbar puncture showed a clear fluid under normal pressure. The cerebrospinal fluid contained 3 cells per c.mm.; the protein was 0.04%; and the Wassermann reaction and Lange curve were negative.

Discussion

Zoster Generalisatus and its Relation to Varicella

The occurrence of a varicelliform rash in the course of herpes zoster is a well-recognized entity. It is variously referred to as zoster generalisatus, zoster universalis, and varicelliform zoster. The condition was probably first described by Tenneson in 1893, and many examples have been recorded since. Minet and Leclercq (1911) collected 25 cases, and Parkes Weber (1913, 1916a, 1916b) described several cases and quoted 20 references. Most reports stress its occurrence in elderly patients. The extent of the eruption varies from the presence of a few aberrant vesicles to a diffuse eruption indistinguishable from the exanthem of varicella. The rash in Case 2, described above, was typical of varicella. Case 3 was not seen in the acute phase of the disease, but the eruption was evidently so like that of varicella that the patient was transferred to an isolation hospital.

The condition is of particular interest in that it provides a no-man's-land in the perennial battle between the monists and the dualists over the relationship between zoster and varicella. It has been assumed by some writers that the eruption constitutes a true attack of chicken-pox (Allen, 1944; Manning, 1944; Sharpe, 1946; and others), or that the concurrence of the two conditions is proof that zoster and varicella are but phases of one and the same disease (Le Feuvre, 1917). But, as Parkes Weber (1916a) has pointed out, this conclusion is hardly justified, as some of the cases show only a few aberrant vesicles, and evidence of an increase in cases of zoster during epidemics of varicella is lacking.

The experimental work of Kundratitz (1925) and Bruusgaard (1932) has an important bearing on this issue. These writers showed that the inoculation of children with vesicle fluid from cases of zoster produced a quasi-varicella rash and that contacts with these children also developed an eruption indistinguishable from varicella. Bruusgaard draws no definite conclusions from this work, but points out that the findings are compatible with the postulate of Haslund (1900) that the difference in the manifestations of infection with the zoster virus might well depend on the portal of entry. Haslund suggested that in zoster the virus gains access to the body via the nasopharynx and spreads to the nervous system, and that the generalized eruption is due to haematogenous dissemination to the skin.

The problem of the relationship between the two diseases is clearly not proved (cp. Wilson, 1940) and will remain so until further facts accumulate. Such data will become available only as the result of systematic investigations, and two lines of approach seem possible. The first is an extension of the work of Aitken and Brain (1933) on the complement-fixation test for the zoster virus, which they found to be positive in all of nine cases of zoster. Application of this test to cases of varicella does not seem to have been undertaken. The second line of approach, suggested by Le Feuvre (1917) and Taylor (1945), is the compulsory notification of herpes zoster, so that its epidemiology might be compared with that of varicella. From observations made in a relatively isolated community Pickles (1939) showed that the epidemic peaks of the two diseases roughly correspond.

Motor Symptoms in Zoster

Of considerable interest and importance are the rare cases of zoster in the course of which the motor nervous system is affected. Involvement of the upper motor neurones has been described (Parkes Weber, 1915), and references to this condition are given by Carter and Dunlop (1941). The majority of recorded cases, however, refer to lesions of the lower motor neurones. These lower motor neurone pareses may be conveniently divided into three clinical types: facial palsy, oculomotor paresis, and segmental spinal-cord paralysis. The three cases described above provide one example of each of these types. As will be seen in the discussion that follows, the mechanism of the production of the motor symptoms is probably different in the three types. In facial palsy the motor fibres are incidentally involved in their transit through the geniculate ganglion, oculomotor lesions arise from peripheral spread of the infection, and spinal paralyses are probably due to actual involvement of the spinal cord by the zoster virus.

Facial palsy is by far the commonest of the motor lesions (Hunt, 1909). It was first clearly described by Ramsay Hunt (1907), and the syndrome often goes by his name. The primary lesion is in the geniculate ganglion, and the herpetic eruption occurs in the cone-shaped area of the cutaneous distribution of the facial nerve, which includes the posterior portion of the tympanic membrane and the external canal, the concha, the antitragus, and the antihelix. In addition to this classical syndrome, facial palsy occurs as a complication of trigeminal herpes (Wilson, 1940; Spillane, 1941). In such cases presumably the Gasserian and geniculate ganglia are affected simultaneously.

An important group of cases is that in which trigeminal herpes occurs with facial palsy but without herpetic eruption in the seventh-nerve distribution. In these cases, of which Case 3 is an example, it has been suggested that the inflammation of the geniculate ganglion is extensive enough to produce paresis, but not to produce herpes (Sharpe, 1915). The significance of these cases is that they provide examples of "zoster sine herpete" of the geniculate ganglion, with abundant evidence of zoster of the neighbouring ganglia. It is but a short step to the assumption that certain cases of "idiopathic" Bell's palsy might be formes frustes of zoster. Ample substantiation of this supposition is to be found in the work of Aitken and Brain (1933), who demonstrated a positive complement-fixation reaction for zoster in four out of 22 cases of facial palsy in which there was no rash. Spillane (1941) brought other evidence to bear in support of this concept when he described a small epidemic of zoster in the course of which a single case of Bell's palsy was seen.

When oculomotor palsy occurs in the course of zoster it does so invariably as a complication of zoster ophthalmicus. The condition was probably first described by Vernon in 1868, and cases were later reported by Hall (1903), Mules (1903), and Parkes Weber (1916a, 1916b). The paresis may be slight, as in Case 2, in which ptosis was the sole manifestation, or more severe, producing complete paresis of the muscles supplied by the third, fourth, or sixth nerves (Hunt, 1909; Carmody, 1937). The clinical aspect is fully reviewed by Edgerton (1942). According to Kinnier Wilson (1940) the probable mechanism of its production is that spread takes place via the small communicating fibres between the first division of the

trigeminal nerve and the oculomotor nerves in the wall of the cavernous sinus. From analogy with geniculate zoster it is tempting to assume that certain of the oculomotor paralyses, especially when associated with ophthalmic neuralgia, might be due to "zoster sine herpete." No work seems to have been done on the complement-fixation test in such cases. It is of interest to note that this possibility was suggested by Mules (1903) some years before the classical work on geniculate zoster by Ramsay Hunt (1907).

Segmental paralysis of spinal-root distribution is rare in the course of zoster, but the complication was clearly described by Sir William Broadbent (1866), who reported a case in which paralysis of the arm followed herpes of the arm and neck. Joffroy (1882) described two cases—one affecting the deltoid and the other the small muscles of the hand. Most of the reports of cases describe cervical segment paralysis (Buzzard, 1902; Wilson, 1940), but involvement of the abdominal muscles (Taylor, 1895) and of the leg muscles (Carter and Dunlop, 1941) has been recorded. In Case 1, reported above, the cutaneous rash and the paralysis were in the distribution of the fifth cervical segment. Recovery was practically complete in three months from the onset. That the prognosis is not always so good is indicated by Carter and Dunlop (1941), in neither of whose cases had complete recovery taken place in nine months to one year.

These cases of segmental motor paralysis throw further light on the pathology of herpes zoster. The primary lesion in zoster is usually to be found in the posterior root ganglion. Head and Campbell (1900), in a study of the post-mortem changes, demonstrated that these ganglia showed round-cell infiltration, haemorrhage, and cell necrosis. They concluded that the changes in the posterior roots and horns and in the peripheral nerves were secondary and degenerative. This is undoubtedly the common state of affairs, but it fails to explain the rare cases in which there is definite clinical evidence of motor-root lesions. Further light is thrown on this problem by the work of Lhermitte and Nicolas (1924). These authors examined the spinal cord of a patient who died of an incidental disease seven weeks after an acute attack of zoster. In this case there was, in addition to the perivascular infiltration and demyelination in the posterior horns, marked evidence of inflammatory changes in the anterior horns. In spite of this there had been no clinical mention of a motor lesion. This finding confirms affection of the anterior and posterior horns of the spinal cord, and the presence of cord inflammation is borne out by the lymphocytosis and the increase in the protein content of the cerebrospinal fluid which commonly occurs (Wilson, 1940; Carter and Dunlop, 1941). The pleocytosis of the cerebrospinal fluid, the clinical manifestations of motor segmental paralyses, and the anterior horn changes in these cases bear a striking resemblance to those found in poliomyelitis. Parkes Weber (1916a) has taken this analogy even further by suggesting that the two diseases may in fact be caused by the same virus. As evidence he quoted the occasional appearance of the diffuse herpes in certain cases of poliomyelitis and the concurrence of epidemics of the two diseases. Further, he suggested that certain cases of painful muscle paresis of obscure aetiology might be regarded as cases of "zoster sine herpete."

Conclusions

In causing infection of the human body the herpes zoster virus shows a predilection for nervous tissue and the skin. In the classical form the brunt of the infection is borne by the sensory ganglia, the resulting symptoms being pain and a cutaneous eruption in the peripheral distribution of the fibres proceeding from the affected ganglia. Study of the rarer manifestations of the disease shows that the infection often spreads beyond these confines. In some cases in which motor symptoms occur there is clinical and pathological evidence that the anterior horn cells of the spinal cord are affected in a manner similar to that in poliomyelitis. In others the infection produces an exanthem clinically identical with that of varicella.

From the available evidence it seems no more reasonable to deduce that varicella and zoster are caused by the same virus than it would be to make a similar deduction regarding zoster and poliomyelitis. It seems much more probable that the virus is capable of producing a range of clinical manifestations varying from simple motor lesions on the one hand to generalized skin lesions on the other, and that the classical form of the disease lies midway between these extremes. This clinical range might be represented as follows: poliomyelitis-like illness—zoster sine herpete—herpes zoster with paralysis—classical herpes zoster—herpes zoster with generalized eruption—varicelliform zoster (sine herpete). This suggestion is of course speculative, and it takes no account of the encephalitic symptoms which are said to occur. Nevertheless, clinically proved examples of each group are to be found in the literature, with the exception of the hypothetical poliomyelitis-like illness, and it is unlikely that evidence of this will be found in the absence of specific complement-fixation tests on such cases.

Summary

Three cases of herpes zoster showing unusual motor and cutaneous manifestations are described. It is suggested that the zoster virus produces a pleomorphic group of diseases with varying degrees of cutaneous and nervous symptoms. Further evidence on certain aspects of the disease could be obtained by immunological and epidemiological investigations.

I wish to thank Dr. E. R. Cullinan for permission to publish Case 3, Dr. A. W. Spence for permission to publish Case 1, and Dr. Paul Abbey for his assistance in Case 2.

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TREATMENT OF CHRONIC ULCERATION AFTER IRRADIATION OF PLANTAR WART

BY

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The plantar wart is commonly cured by irradiation. In wartime the condition was a frequent cause of minor disability in the Services, and was treated by radiotherapy under out-patient arrangements. A record of dosage sometimes failed to follow the patient on his travels; and overexposure undoubtedly occurred in some instances. Chronic intractable ulceration of the sole resulted in prolonged disability out of all proportion to the importance of the original lesion.

The ulcer heals slowly or not at all when treated with recumbency and local applications. Deep fibrosis leads to an unstable tender scar on the sole which prevents normal walking. Recurrence follows simple excision performed without skin replacement. A "free" skin-graft is unlikely to provide a permanent cover in this situation even if it succeeds on the relatively avascular base. Local pedicled flaps are as unsatisfactory on the sole as they are on the palm.

Radical excision down to healthy tissue and outwards to normal skin, however, leaves a defect which can readily be filled by means of a direct pedicled flap from the opposite leg. This provides a stable skin cover with a subcutaneous pad. The patient can walk in normal shoes without pain in six to eight weeks. It should be emphasized that this method of treatment is advised for ulceration which results in all probability from the radiation itself, and not for that which may follow repeated attempts to eradicate the plantar wart by mechanical, thermal, and chemical means.

Case 1

A married woman aged 36 complained of an extremely tender ulcer on the sole of the foot. The ulcer had persisted for two and a half years after a repeated application of deep *x*-ray therapy to a plantar wart. Excision had been performed more than once, and many remedies had been applied locally. The ulcer varied in size and in degree of infection, but had never healed.

When seen on Sept. 4, 1944, the ulcer was 1/2 in. (1.25 cm.) in diameter, had an indolent rolled edge, but was relatively free from infection after treatment with penicillin cream during a recent puerperium. A haemolytic staphylococcus was cultured.

On Sept. 7 the ulcer was excised down to healthy plantar fascia and a margin of apparently healthy skin was included; a pedicled flap was raised from the opposite leg to fill the defect. A five-day systemic course of penicillin was given. The pedicle was separated and the flap implanted on Sept. 26. Healing was rapid. The patient left hospital able to walk in normal shoes on Nov. 3.

The pathologist's report was as follows: "The skin changes are compatible with irradiation dermatitis (hyperkeratosis, obliterative endarteritis, and atrophic changes in accessory skin structures), followed by superficial ulceration and subcutaneous fibrosis. There is no evidence of malignant change in the section examined."

Case 2

A soldier aged 34 had suffered from the effects of a plantar wart since 1943. This had been pared by a chiropodist, excised at least four times in different hospitals, and cauterized. The ulcer had been treated with permanganate, salicylic acid, vitriol, formalin, flavine, eusol, gentian violet, penicillin cream, and several other less certain substances. Deep *x*-ray treatment had been given at more than one hospital, and in several doses.

FIG. 1.—The ulcer in Case 2.

When seen on July 12, 1946, there was an ulcer on the sole of the right foot, 1¼ in. (3 cm.) in diameter (Fig. 1). The base consisted of firm tender granulations with a yellow slough. The edge was indolent and blue in colour, and was surrounded by an area of dusky induration. The Wassermann reaction was negative.

The ulcer was excised on July 29 and the defect, which extended down to plantar fascia and measured 2 in. (5 cm.) square, was filled by means of a direct pedicled flap from the

FIG. 2.—Application of a pedicled flap from the opposite leg.

opposite leg (Fig. 2). The secondary defect of the donor leg was closed by a dermatome graft from the thigh. A systemic course of penicillin was administered for five days.

The pedicle was divided on Aug. 23, and the flap implanted. The patient began to walk after a course of physiotherapy. He went before the medical board on Oct. 24 and was discharged

FIG. 3.—Showing the foot soundly healed.

from the Army. The foot was soundly healed (Fig. 3). The pathologist's report was: "Portion of skin shows ulceration with fibrinoid necrosis in the floor of the ulcer."

EXERTION HAEMOGLOBINURIA

REPORT OF A CASE

BY

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The form of paroxysmal haemoglobinuria associated with exertion is rare and its pathology is imperfectly understood. The clinical features and the results of laboratory investigations undertaken in a case studied by us are here recorded.

Case History

The patient, a European sergeant aged 33, first came under our observation at the end of July, 1944, when he was seen as an out-patient by one of us. He brought with him a sample of almost black urine which he had passed after playing a game of football. He gave the following interesting history.

In civil life he had worked as a stevedore and had never noticed any urinary abnormality or suffered from any illness. In September, 1940, on returning to the U.K. from France, he noticed that after a cross-country run his urine was dark. The same occurrence was noticed on two subsequent occasions under similar circumstances. He then remained free from symptoms until June, 1942, when again after a run his urine was dark. He was admitted to hospital for investigation, the results of which are not known to us, but his medical category was lowered to B. In June, 1943, his category was raised to A again, as he was eager for service afloat. In June, 1944, he arrived in East Africa, and early in July, after a route march, he had his first recurrence of the old symptom. On July 27 he played football, and it was a sample of the urine passed after this game that he brought with him to hospital. Examination of this specimen of urine showed: colour very dark brown; reaction acid; albumin ++++; benzidine test ++; deposit: a few red blood cells, granular casts +, urates ++, a few calcium oxalate crystals.

He was admitted to hospital on July 31 for further investigation. It was established that a 20-minutes run invariably resulted in a paroxysm of haemoglobinuria lasting several hours. No constitutional disturbance accompanied the paroxysms, but there was some aching in the back and abdomen. The patient was of good physique; no other signs of disease were detected, and before an attack the urine contained nothing abnormal. It was decided to lower his medical category to C for six months, and he was discharged to duty in this category on Aug. 30.

During the next three months the patient reported that the paroxysms were becoming more frequent and that less exertion was required to produce them. Actions such as hauling on ropes were now apt to be followed by an attack, and the condition was becoming a liability in his daily work. He was readmitted to hospital on Nov. 29, and the investigations detailed in Table I were carried out.

An attempt was made to demonstrate the presence of intravascular haemolysins. The patient's red blood corpuscles and serum were mixed and incubated at 37° C. for two hours, with and without previous exposure to a temperature of 4° C. for 30 minutes, and with and without added complement (Donath–Landsteiner reaction). Foreign group O cells and patient's serum, and patient's cells and foreign serum, were also set up against each other in a similar manner. All these tests were carried out on blood taken from the patient 3 minutes, 15 minutes, and 30 minutes after the beginning of a 30-minute run, and then 45 minutes, 90 minutes, and 7 hours after the exercise was finished. Haemolysis *in vitro* was not demonstrated in any of these tests, or in tests for haemolysin on small amounts of fluid aspirated from muscle during and after exercise. Examination of urine taken at intervals after the beginning of exercise gave the results shown in Table II.

TABLE I.—*Results of Tests Before and Immediately After a 30-minute Run*

Test	Before Exercise	After Exercise
Haemoglobin (Sahli)	120%	106%
Red cells	5,750,000/c.mm.	5,320,000/c.mm.
White cells	9,000/c.mm.	8,400/c.mm.
Neutrophils	74%	78%
Lymphocytes	19%	18%
Monocytes	5%	3%
Eosinophils	2%	0·5%
Basophils	—	0·5%
Primitive white and red cells	Nil	Nil
Platelets	545,000/c.mm.	475,000/c.mm.
Coagulation time (at 30° C.)	5 minutes	6 minutes
Bleeding time	60 seconds	60 seconds
Reticulocytes	0·6%	0·4%
Blood group	O	O
Fragility of red cells	Total lysis in 0·34% NaCl; no lysis in 0·42% NaCl (within normal limits)	Total lysis in 0·32% NaCl; no lysis in 0·42% NaCl (within normal limits)
Packed cell volume	41%	40%
Mean corpuscular diameter	6·8μ	6·8μ
" " volume	71 c.μ	75 c.μ
" " average thickness	1·9μ	2·1 μ
Van den Bergh reaction	Direct, nil. Indirect, 1·6 units	Marked haemolysis
Icterus index	6·6	

A rising and falling curve of oxyhaemoglobinaemia, which approximately paralleled the curve of haemoglobinuria, was demonstrated by tests on blood taken at intervals during and after exertion. It was possible to make only a rough estimate of haemoglobin by Sahli's method; the figures obtained are shown in Table III. The absorption spectrum for pseudomethaemoglobin was not found in any of the sera examined.

TABLE III

Time Since Exercise Began:	During Exercise			After Exercise		
	3 min.	15 min.	30 min.	75 min.	120 min.	450 min.
% Hb (Sahli)	Less than 0·2	0·5	1·5	1	0·2	Less than 0·2
Hb (calculated from Sahli)	Less than 34 mg.	85 mg.	255 mg.	170 mg.	34 mg.	Less than 34 mg.

The following experiment was performed in an attempt to determine if haemolysis occurs locally in muscle during exercise. First, 5 ml. of blood was withdrawn from a vein in the right arm and allowed to clot. A sphygmomanometer cuff was then applied to the left upper arm and inflated to a pressure of 100 mm. Hg. The patient then exercised the left arm, alternately extending and flexing the wrist and fingers for two minutes. At the end of this time blood was withdrawn from a vein in the left arm, with the sphygmomanometer cuff inflated. The serum from these two specimens showed no perceptible difference in colour. The experiment was repeated, this time releasing the cuff just before blood was withdrawn; the specimen presumably contained blood from all parts of the occluded limb, and it, too, showed no trace of haemolysis.

TABLE II.—*Results of Urine Examinations*

Hours after Exercise Started	Appearance	Spectroscopy	Protein	Sugar	Deposit
1/2	Dark brown, turbid	Oxyhaemoglobin ++; methaemoglobin +++	++++	Nil	Granular casts +++; epithelial and pus cells +
1	Dark brown, very turbid	Methaemoglobin ++++	++++	"	Granular casts and epithelial and pus cells +
1½	Dark brown, turbid	Methaemoglobin ++	+	"	Granular casts and epithelial cells +
3	Brown	Methaemoglobin ++	+	"	" " "
5	Pale brown, slightly turbid	Methaemoglobin +	Trace	"	Epithelial cells +
7	Amber, clear	No blood pigment	"	"	Pus cells and epithelial cells +
24	" "	" "	"	"	" "

Finally it was decided to test the effect of posture. The patient stated that 20 minutes' vigorous swimming had not precipitated an attack. In our experiment he was instructed to "cycle" on his back, supporting his buttocks on his hands, his flexed elbows resting on the bed. This position over-corrected any possible lordosis. After 10 minutes' vigorous exercise in this position blood was withdrawn from a vein. The serum from this specimen showed no trace of haemolysis, and urine passed shortly afterwards was also clear of protein and of haemoglobin derivatives.

Discussion

Our experiments support the view that exertion haemoglobinuria results from haemolysis during exertion in the erect or extended position. This agrees with the common view. Cases, however, seem to vary in their degree of dependence on the postural factor. Thus in the case recorded by Makin (1944) haemoglobinuria was strictly postural, and did not occur after exercise on a bicycle, whereas in the case recorded by Witts (1936) running with bent back and work on the bicycle ergometer were followed by haemoglobinuria. The postural factor and the common association with lordosis suggest that the condition is allied to orthostatic albuminuria. Bicycle exercise in Makin's case was followed by albuminuria but not by haemoglobinuria. Orthostatic albuminuria was not present in our case.

The failure to demonstrate circulating haemolysin is of little significance and does not rule out the occurrence of intravascular haemolysis; for unless combination with red cells is prevented by special factors, as it is in the case of cold haemoglobinuria, haemolysin liberated into the circulation is likely to be fixed rapidly. In nocturnal haemoglobinuria all efforts to demonstrate circulating haemolysin have failed (Witts, 1936). The failure to demonstrate local haemolysin in muscle is in keeping with the postural features of the disorder and with the view of Witts, who regards the kidney as the source of the haemolysin. He considers intravascular haemolysis "hardly conceivable" in view of the absence of anaemia and the slightness of systemic changes and of haemoglobinaemia; he regards a local haemolysis in the vessels of the kidney as more probable.

According to Whitby and Britton (1944), in exertion haemoglobinuria "there are neither the constitutional symptoms nor the haemoglobinaemia so characteristic of haemoglobinuria from cold." In our case there was a cherry-red concentration of haemoglobin in the serum, and it would seem that the lowering of the blood haemoglobin level was slight because haemolysis was of short duration only, accompanying tiring exertion in the vertical posture. Whitby and Britton state that in cold haemoglobinuria haemoglobin appears in the urine when the free haemoglobin in the plasma exceeds 100 to 140 mg. per 100 ml. This is higher than the plasma haemoglobin level recorded after exercise in Witts's case (46.5 mg.) but considerably lower than that recorded in ours.

History of an injury is another inconstant feature in exertion haemoglobinuria, which, however, helps to incriminate an abnormal kidney as the immediate cause of haemolysin production. No history of injury was elicited in our case, but the disease had come on rather suddenly shortly after a campaign, when slight injuries might have been ignored. In contrast to the usual history, our case resembled that of Witts in showing symptoms for a period (with intermissions) of considerably more than one year. The age at onset of the complaint was much above the average, and it is of interest that the condition recurred with unusual severity when the patient came to the Tropics.

Summary

A case of paroxysmal haemoglobinuria of exertion is described.

Laboratory investigations, including attempts to demonstrate circulating haemolysin, are described and discussed.

Our thanks are due to Brig. R. Cormack, D.M.S., E.A. Command, for permission to submit this article for publication.

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"TRIDIONE" IN THE TREATMENT OF PETIT MAL

BY

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Tridione, the synthetic anticonvulsant drug (3,5,5-trimethyloxazolidine-2,4-dione), has been extensively used in the treatment of the petit-mal epilepsies by investigators in America since 1944.

A Preliminary Investigation

Recently, when supplies became available in this country, a preliminary investigation was made at St. David's Hospital (for epilepsy), the findings of which are tabulated below. Most of the patients (who are sane males suffering from idiopathic epilepsy, and whose ages range from 17 to 56) have been taking the drug for three months.

Tridione is supplied in 0.3 g. capsules. So far it has been found that the apparently optimum dose in the average case is four capsules daily, in divided doses. One patient aged 17, however, has had his petit-mal attacks abolished by taking only two capsules daily. The drug was given in addition to other medication, such as phenobarbitone and "epanutin" (soluble phenytoin), which the patients had previously been taking.

Convulsive seizures of the grand-mal type did not appear to be reduced by tridione in any case, and one man experienced, possibly as a coincidence, an increase in the number of his fits. All the patients suffered from petit-mal except one whose seizures were of the myoclonic type. This man's condition did not improve. Another, however, who had myoclonic spasms as well as ordinary petit mal, states that he feels better than he has done for years.

It is possible that the patients who showed no improvement might have been benefited had they been given more than six capsules daily. Unfortunately a shortage of supplies precluded an increase of this dose.

No. of patients	23
Entirely free from petit mal	4 (17.4%)
Petit mal reduced by more than half	12 (52.2%)
Definite but slighter improvement	2 (8.7%)
No improvement, or toxic symptoms necessitating withdrawal of drug	5 (21.7%)

Because of the notorious difficulty in obtaining an accurate record of petit-mal attacks each patient was given a notebook, and in this he marked down every attack of which he was aware, or which any fellow patient or member of the nursing staff observed. For the purpose of comparison the patients had kept similar records of their attacks for a period of two months before starting tridione medication.

A few days after beginning to take the drug approximately four-fifths of the patients reported a reduction in the number of their petit-mal attacks. After a week or 10 days no fewer than 19 of the 23 patients mentioned that on walking out of a building into the open air they found the

light too bright. This phenomenon was variously described as "dazzle," or "glare," or "a whiteness like mist over everything." Some patients stated that they found reading in the open air to be impossible, and others said that objects appeared to have changed colour, as, for example, a familiar blue motor-car seemed to be cream-coloured. In most instances the sensation ceased after a short interval, but 10 of the men found it trying and were glad to wear dark glasses to mitigate the effect.

Five men were aware of slight drowsiness, apparently due to the drug; one complained of lack of concentration, and one of restlessness. Two developed slight ataxia; two complained of hiccup, and two of slight epigastric discomfort. One developed a slight rash, similar to acne, on the face; and one, whether *post* or *propter hoc*, had a severe rash of the face, neck, and hands which initially looked like urticaria and proceeded to an acute dermatitis with exudation and desquamation. In this case the drug was withdrawn, as it was in four others in which, although no marked toxic symptoms were present, there appeared to be no improvement in the incidence of petit mal. Most of the other 18 patients were anxious to continue taking the drug, as in their opinion the relief obtained from the reduction in their attacks more than outweighed the slight nuisance of the "dazzle phenomenon" or the other symptoms mentioned above.

Comment

Several important points emerge from a review of some of the literature on the subject. Tridione is said to be contraindicated in patients with severe renal or hepatic damage and in conditions in which optic-nerve disease is already present; but no residual damage to the optic nerve has been detected in patients complaining of the "dazzle phenomenon"; and "histological studies on the optic nerves and retinae of experimental animals receiving large doses of tridione over long periods have failed to reveal any evidence of damage." Several investigators have also recorded that when the drug is withdrawn weeks or months may elapse before attacks of petit mal return.

Obviously more time and greater experience are required before this drug can properly be evaluated, but there is no doubt that tridione has a pronounced inhibitory effect on petit mal and also, in the experience of American investigators, on myoclonic spasms and akinetic seizures.

Summary

The treatment by tridione of 23 cases of the petit-mal epilepsies is analysed.

Approximately four-fifths of the patients improved, but various toxic symptoms and signs were manifested in almost every case.

I wish to express my cordial thanks to the male nurses of St. David's Hospital for their keen and efficient co-operation in conducting this investigation.

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The Merseyside Hospitals Council Report for 1946, *Carefree Convalescence*, is a pleasantly illustrated pamphlet with a brief account of the after-care arrangements that the Council has developed during the last twenty years. The Council has continued to acquire houses for convalescent homes, and suggests that the increasing demand for such facilities likely to rise under the National Health Service might be met in part by voluntary assistance. Four members of the Council have been appointed to the Liverpool Regional Hospital Board.

Medical Memoranda

A Fatal Case of Agranulocytosis Associated with "Tridione" Therapy

Now that tridione is being used for the treatment of certain types of epilepsy it is of interest to record the following case. This substance seems to have a high therapeutic value. Nevertheless, until extended use of it proves otherwise, it seems that it should be used with care owing to a possible depressant action on the granulocyte precursors in the bone marrow.

CASE HISTORY

A boy aged 11 had suffered from petit mal for over three years, during which time he had received amphetamine sulphate ("benzedrine") in doses of 0.01 to 0.025 g. daily. For 53 days he received four 0.3-g. tablets of tridione daily. On the 25th day of receiving tridione he developed an urticarial rash on the thighs which faded in two days. On the 51st day of tridione therapy he became ill with gingivitis and a temperature. He lived for 21 days after ceasing tridione. He received sulphathiazole (a small total amount) and penicillin by injection without any helpful effect.

When examined nine days before death he repeatedly complained of sore throat, and was very pale. The mucous membranes were a good colour, the gums were hypertrophied a little and very red, the tongue was furred and had an ulcer on the left margin. The fauces were somewhat red, but there was no lesion. The upper and lower cervical glands and a gland on the edge of the jaw were enlarged. The left submaxillary gland was enlarged and painful. The trachea was pushed to the right. There was tenderness in the right iliac fossa, where a movable tumour 2 by 2 in. (5 by 5 cm.) was felt. The spleen was slightly enlarged, as were the glands in the groins and axillae.

A radiograph of the chest revealed a shadow in the mediastinum displacing the trachea to the right. A blood count showed: Hb, 44%; R.B.C., 2,730,000; colour index, 0.8; W.B.C., 800 per c.mm. A differential count showed: all lymphocytes and no granulocytes; there were abundant platelets; after a prolonged search no "blast" cells were seen; all the white cells were mononuclears in type, and immature. A trace of albumin was present in the urine. A sternal puncture marrow smear revealed an aplasia of the erythroblastic tissue with a primary agranulocytosis.

Treatment consisted of blood transfusion and administration of pyridoxin and plexan. For two days before death he had profuse yellow diarrhoea. Later blood examination showed no change.

Abnormal Post-mortem Findings.—Bowel: Small yellow sloughing ulcers in lower foot or so of ileum in Peyer's patches, which were hyperplastic; gross swelling, redness, and ulceration of lower 3 in. (7.5 cm.) of small bowel, ileo-caecal valve, and caecum; multiple yellow ulcers in ascending colon; mesenteric glands +. *Liver:* Dark from free iron +. *Spleen:* Enlarged; free iron +. *Suprarenals:* Greyish with little lipoid. *Brain:* Greyish, especially cortex. *Bone*: Dark-red marrow in sternum, ribs, vertebrae, femur.

Microscopical Findings from Post-mortem Material.—The tumour in the right iliac fossa showed non-specific ulceration and gross oedema. *Lumbar vertebra section:* Macroscopically the bone marrow is very red; microscopically there is some erythroblastic (normoblastic) hyperplasia, an almost complete absence of myeloid elements, and an approximately normal number of megakaryocytes.

COMMENTARY

The bone section shows that a complete aplasia of the granulocyte precursors in the marrow had supervened. The amount of sulphathiazole seems much too small to have caused this depression (over 30 g. has usually been taken in agranulocytosis due to sulphonamides). Tridione is strongly inculpated. It will be noticed that about half-way through his tridione course (25th day) the patient developed a rash. Two other children on tridione for epilepsy developed rashes and diffuse lymph-gland enlargement. In their case tridione was stopped immediately the rash appeared, and they recovered uneventfully without abnormality in the blood picture.

If during the course of tridione therapy any generalized rash, lymphatic enlargement, undue redness of gums, anaemia, or changes in the white cell count appear it would be wise to cease using tridione.

I have to thank Dr. E. A. Hunter, senior physician in charge of the case, for permission to publish and Dr. T. N. Gledhill for his report on the marrow section.

R. F. BRAITHWAITE, M.R.C.S., L.R.C.P.

Reviews

CHILD HEALTH

Child Health and Development. By Various Authors. Edited by Richard W. B. Ellis, M.D., F.R.C.P. (Pp. 364; 49 illustrations. 18s.) London: J. and A. Churchill. 1947.

This book is a valuable addition to the growing library of books on child health, and the editor has been fortunate in the authority and special knowledge of the twelve other contributors to the volume. Of its two sections the first—on development—contains an account of anatomical, physiological, and psychological aspects of growth. We would draw attention to the masterly chapter on functional development of the foetus, by the late Sir Joseph Barcroft, and those on growth and puberty by Prof. H. A. Harris and by the editor. Prof. Ellis also contributes to this section two chapters on the newborn and on digestion, nutrition, and feeding, in which he combines in a clear and concise narrative essential scientific knowledge with practical guidance. The second section, "Social Aspects of Child Health," is considerably shorter and is mainly devoted to brief accounts of the social services and institutions dealing with healthy, "deprived," and delinquent children. It also includes a short account of the English educational system by Sir Fred Clarke.

The unfolding and complicated life of the growing child in all its aspects, together with the social problems that are involved, is a vast subject, and we cannot expect a book of this modest size to contain a full account. It is also difficult to give unity to a book of composite authorship. But all who have the care of children will welcome this book; it is a scientific manual and makes fundamental scientific knowledge available for the practical guidance and control of child health.

CHARLES MCNEIL.

TREATMENT OF DELINQUENCY

The Psycho-analytical Approach to Juvenile Delinquency. Theory, Case Studies, Treatment. By Kate Friedlander, M.D., D.P.M. International Library of Sociology and Social Reconstruction. (Pp. 296. 18s.) London: Kegan Paul, Trench, Trubner and Co. 1947.

Although a steadily increasing amount of work has been done on the psychological aspects of delinquency, so much indeed that the clinical diagnosis and treatment of delinquency can now be regarded as a special branch of medical psychology, there is an astonishing dearth of reliable textbooks on the subject. Dr. Friedlander's book goes far to remedy this defect. That it is written by a thorough-paced Freudian is not altogether inappropriate, for without Freud's discoveries of the unconscious mind and of the unconscious mechanisms that regulate it the field of delinquency must have remained a *terra incognita.*

Despite the fact that the author devotes a substantial part of her book to presenting psycho-analytical theory and is throughout clearly influenced by psycho-analytical opinions, the scope and method of her presentation give evidence of first-hand clinical experience. In the section on diagnosis she clearly distinguishes unconscious factors from those social factors which not only influence the development of antisocial conduct but often determine its immediate direction. Indeed, she bases her classifications of delinquent states largely on these distinctions. Perhaps here she is least convincing. Like many analysts she pays scant attention to the clinical concept of psychopathy, a neglect which is justified only if psycho-analysts can produce more illuminating and at the same time more useful clinical classifications of character disorder. They do not appear to have done this.

Discussing treatment, Dr. Friedlander carefully distinguishes between psycho-analytic and other forms of psychotherapy and points out the limitations to applying classical psycho-analytic methods to delinquent subjects. She describes clearly the role of "transference" in the various forms of social therapy or disposal and ends with a useful outline of preventive measures. This is a good book.

EDWARD GLOVER.

EXTRACELLULAR FLUID

Chemical Anatomy, Physiology and Pathology of Extracellular Fluid. A Lecture Syllabus. By James L. Gamble. Fifth edition. (Pp. 160. 52 charts. 7s. 6d.) Cambridge, Mass.: Harvard University Press. London: Geoffrey Cumberlege (Oxford University Press). 1947.

Prof. Gamble's monograph is now established as being one of those few medical books which may truly be described as classics. As in previous editions he modestly presents the material as a syllabus of concise lecture notes based on illustrative charts; thus each section is simply headed with the number of a chart, which is explained in the text. This manner of exposition from simple line diagrams enables the author to make complex biochemical subjects easily understandable to the general medical reader. The text is brief, occupying 105 pages in large print, but characterized by remarkable lucidity and by flashes of inspired phrasing.

The main feature of the book is that the author amplifies and gives precision to Claude Bernard's great concept of the internal environment. Prof. Gamble, largely on the basis of his own research, has revealed the essential qualitative and quantitative aspects of the extracellular fluid. His separate papers and this integrated presentation illumine and make real a subject, hitherto dimly understood, which is not only important in the theory of physiology and pathology but of great practical significance in a wide range of medical and surgical disorders. To quote but one example: understanding of the normal and abnormal states of the extracellular fluid is fundamental to the proper use of fluid administration whether by mouth or by parenteral routes. The construction of the book is similar to that of former editions, but it contains some new material. The author begins by describing the normal quantity and composition of the extracellular fluid and then goes on to discuss how its constancy of composition and volume are maintained. In the later part of the book he considers the pathogenesis of dehydration and of acidosis and alkalosis and, finally, parenteral fluid therapy.

H. L. MARRIOTT.

RADIOLOGY

Radiography for Medical Students. By Fred Jenner Hodges, M.D., Isadore Lampe, M.D., and John Floyd Holt, M.D. (Pp. 424; 103 plates. $6.75 or 37s. 6d.) Chicago: Year Book Publishers, Inc. London: H. K. Lewis and Co. 1947.

Confrontations. Radio-Anatomo-Cliniques. Published under the direction of M. Chiray, R. K. Gutmann, and J. Sénèque. Fascicule I. (Pp. 56; 98 figures. 370 francs.) Paris: G. Doin et Cie, Masson et Cie. 1946.

The undergraduate teaching of radiology in Britain is essentially elementary and in most medical schools does not consist of more than half a dozen lectures a year; it is debatable whether more should be packed into the already overloaded curriculum. Radiology is now sometimes taught with anatomy and physiology, and some of the pioneers argue that the combination is particularly instructive. American medicine has gone much further in this direction. This interesting volume, equally divided into accounts of *x*-ray diagnosis and therapy, is founded on the authors' teaching of undergraduates in the University of Michigan. There is no doubt that if the undergraduate has the time and basic knowledge to read and digest its contents he would become a wiser and better doctor, for it is well written and combines a full account of pathology with instruction in elementary radiology and physics. Judged by British standards it contains far too much, and it is not unreasonable to say that the material is so plausibly presented that there is a danger of diverting the student from more fundamental approaches to health and disease. This book is best for the postgraduate student and the beginner in radiology, but something less than this and more than the meagre pittance we consider necessary for the undergraduate is desirable and has still to be written.

The second volume is neither an essay on radiology nor a textbook but a report of the clinical, pathological, and radiological findings in 53 interesting cases of disease of the gastro-intestinal tract. The authors are well known to radiologists for their interesting pre-war contributions to the study of early carcinoma of the stomach. In this series there are many such

cases; they are of considerable interest in that they show how easy it is when certain appearances are present to confuse benign with malignant lesions. With one or two exceptions all the material has been selected because the cases were difficult to diagnose. There are a few striking examples of cholecystography in which the gall-bladder failed to fill after a single dose of radio-opaque substance but concentrated normally when a second dose was given immediately after the first *x*-ray examination. All these case histories are well worth detailed study by radiologists.

PETER KERLEY.

PHYSIOLOGY

Précis de Physiologie. By L. C. Soula. (Pp. 1,086; 334 figures. 1,450 francs.) Paris: Masson et Cie. 1947.

Perusal of this outline of physiology confirms the significance of its dedication to Sir Charles Sherrington. The author claims—and he is probably right—that it is the first treatise on physiology in the French language to be based on the school of neurophysiology that Sherrington founded, and that it brings into accord the traditional outlook of French universities with that of the modern British medical schools. He emphasizes the large part played by new techniques in the transformation undergone by physiology in recent years. His central idea is the unity of the living animal—as he indicates in an admirable introduction—and everywhere he incorporates the recent teachings of general physiology as they throw light on the mechanisms of the human body. The book is well written, thoroughly up to date, and the diagrams are clear and instructive. It is an outline of modern physiology admirably suitable for the student of medicine.

C. LOVATT EVANS.

ASTHMA

The Diagnosis and Treatment of Bronchial Asthma. By Leslie N. Gay, Ph.B., M.D. With foreword by Warfield T. Longcope, M.D. (Pp. 334; 80 illustrations. 27s. 6d.) London: Baillière, Tindall and Cox. 1946.

Handbooks on bronchial asthma come across the Atlantic with such regularity that one is sometimes tempted to ask, "Is your journey really necessary?" A number of features give this book a certain individuality and interest for the general medical reader. Much of its content is a recapitulation of the author's own work, and it is evident that he has had wide experience in this field. The account of pollen surveys is interesting and shows how much work has been done on this important subject in the U.S.A. The chapter on pathology includes post-mortem records of 24 patients dying of asthma at the Johns Hopkins Hospital. In the last 130 pages the author describes the treatment of asthma in a practical and detailed manner, with a complete account of modern methods. The many case histories illustrating certain points in the history or treatment are an important feature of the book; they are helpful but could often be more concise without impairing their usefulness.

The arrangement of the subject matter is sometimes confusing. For example, in discussing the treatment of asthma combined with bronchial infection, the author does not mention penicillin or sulphonamide therapy, though he adequately describes them under a separate heading later on. In Chapter V the accounts of complications and differential diagnoses of bronchial asthma are inextricably mixed, and we cannot see why the effect of anaesthetics should be discussed here at all. Nor is it clear why cases of asthma starting during pregnancy are considered under the heading of "Psychosomatic Syndrome," while those whose symptoms occur during menstruation or at the menopause are regarded as due to "endocrine disorders."

It is surprising to read that Dr. Gay considers that 50% of patients with hay-fever get asthma unless properly treated; in Britain such a figure would certainly be too high. On the other hand readers in this country will be comforted to know that in the author's opinion there is no field of allergy more overrated than so-called gastro-intestinal allergy, and that the "leukopenic index"—a tedious manœuvre for the diagnosis of specific food sensitivity—is inconsistent and unreliable.

R. S. BRUCE PEARSON.

BOOKS RECEIVED

[Review is not precluded by notice here of books recently received]

African Medical Handbook. By Michael Gelfand, M.B., M.R.C.P. (Pp. 202. 15s.) Capetown: The African Bookman. 1947.

An outline of medicine and hospital practice for African nurses and orderlies.

Plough and Pasture. By E. Cecil Curwen, M.A., M.B., F.S.A. (Pp. 122. 7s. 6d.) London: Cobbett Press. 1946.

The early history of agriculture and stock breeding.

Physical Fitness Appraisal and Guidance. By T. K. Cureton, Jr., M.A., M.P.E., Ph.D., *et al.* (Pp. 566. 30s.) London: Henry Kimpton. 1947.

A general account of physique and its measurement.

Psychological Approaches to the Biography of Genius. By L. M. Terman, LL.D., Ph.D., Sc.D. (Pp. 24 1s. 6d.) London: Hamish Hamilton. 1947.

A presidential address delivered before the Pacific Division of the American Association for the Advancement of Science.

Genetics, Medicine, and Man. By H. J. Muller, C. C. Little, and L. H. Snyder. (Pp. 158. 12s. 6d. or $2.25.) Ithaca, New York: Cornell University Press. 1947.

Essays on the gene, heredity, and mutation.

Treatment of Some Chronic and 'Incurable' Diseases. By A. T. Todd, O.B.E., M.B., M.R.C.P. 2nd ed. (Pp. 324. 25s.) Bristol: John Wright and Sons, Ltd.; London: Simpkin Marshall, Ltd. 1947.

Includes discussion of epilepsy, cancer, asthma, diabetes mellitus, constipation and rheumatism.

Operative Gynecology. By Richard W. Te Linde, M.D. (Pp. 751. £5 10s.) London: J. B. Lippincott. 1947.

A profusely illustrated textbook by the professor of gynaecology at Johns Hopkins University.

Hormones and Vitamins. By G. A. Stephens, M.P.S. (Pp. 315 21s.) London: George Newnes, Ltd. 1947.

Compiled to facilitate the prescribing and dispensing of hormones and vitamins.

Handbook of Child Guidance. Edited by Ernest Harms. (Pp. 751. No price.) New York: Child Care Publications. 1947.

Articles on child guidance in America by various authorities.

Psychologie der Suggestie en Autosuggestie. By Dr. Berthold Stokvis. (Pp. 263. 15 Dutch florins.) Lochem: De Tijdstroom. 1947.

A monograph on the psychology of suggestion and hypnosis. In Dutch.

Lehrbuch der Pharmakognosie. By George Karsten and Dr. Ulrich Weber. (Pp. 428. No price.) Vienna: Verlag von Gustav Fischer. 1947.

A textbook of botany for students.

Modern Drugs in General Practice. By Ethel Browning, M.D., Ch.B. 2nd ed. (Pp. 223. 12s. 6d.) London: Edward Arnold and Co. 1947.

An account for medical practitioners of the more recently introduced drugs.

Clinical Dental Roentgenology. By J. O. McCall, D.D.S., F.A.C.D., and S. S. Wald, D.D.S., F.A.C.D. 2nd ed. (Pp. 343. 35s.) London and Philadelphia: W. B. Saunders Co. 1947.

Describes the technique of dental radiography and interpretation of skiagrams.

Nelson Loose-leaf Medicine. Renewal pages. (No price.) Thomas Nelson. 1947.

The Biological Standardisation of the Vitamins. By Katharine H. Coward, D.Sc. 2nd ed. (Pp. 224. 16s.) London: Baillière, Tindall and Cox. 1947.

Discusses the methods of standardization and their statistical evaluation.

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CONSULTANTS AND THE ACT

When changes in the Emergency Medical Service were announced by the Minister of Health in November, 1939, the three distinguished men who were then Presidents of the Royal College of Physicians, Royal College of Surgeons, and Royal College of Obstetricians and Gynaecologists wrote a letter to the *Journal*[1] urging the medical profession to accept the Minister's proposals. In this letter the Presidents sought to allay the fears of those who saw in these proposals the nucleus of a State Medical Service. What they then wrote is worth quoting:

"There is a suspicion amongst some doctors that the Ministry of Health may be proposing to use the E.M.S. as the thin end of the wedge for a post-war State Medical Service. We can assure such, on the highest authority, that nothing is further from the Ministry's intention and that all such fears are groundless. It may well be, of course, that after the war economic conditions may make some form of assistance to the voluntary hospitals, by grants-in-aid or otherwise, necessary, but that the voluntary system will continue there is no reason to doubt."

The Presidents' assurance was of course accepted, just as they, and quite rightly, accepted the assurance of the "highest authority." But, as Dr. Alan Wigfield subsequently pointed out,[2] the assurance must be "based on the assumption that this same Ministry and, indeed, this same Government will be in office when the war is over." Dr. Wigfield went on to say, "Whatever may be the case we must keep before us the possibility that sooner or later a political group for the time being in power may yet seek to introduce a State Medical Service." Dr. Wigfield has proved to be a safe prophet. While recognizing that the voluntary hospitals might need financial assistance, the Presidents undoubtedly believed that they would continue within the framework of the voluntary system. But this is not to be. The voluntary hospitals on July 5 this year will be State hospitals and each will be administered by Boards of Governors the chairmen of which are to be appointed by the Minister of Health. The teaching hospitals, too, it must be emphasized, will be State hospitals. The voluntary system will come to an end, and the State will be the monopoly owner of all voluntary, municipal, and other hospitals the Minister decides to take over on the recommendation of the Regional Hospital Boards.

No one would assert that the hospital service in this country is the best in the best of all possible worlds. The idea of establishing a hospital service on regional lines under the influence of university centres has received widespread professional support. Some plan of efficient co-ordination in hospitals was clearly necessary. Those who were aware of the defects in the vast hospital service administered by the London County Council were, nevertheless, apprehensive of the dangers of too much planning, of too much Government. Yet it is remarkable to note that the existing owners of hospitals and the medical men who work in them have made little effective criticism of the Minister's hospital proposals in the National Health Service Act. So anxious have many been that they should not come under the control of local authorities that they have accepted with some sense of relief the translation of the municipal hospital into the State hospital. Consultants, but by no means all, have accepted the State hospital as the lesser of two evils, and all have been balked by the spectre of hospital finance from thinking further on constructive lines.

Such is the confusion of minds and of tongues in the consultant and hospital world that there is unlikely to be any effective challenge to the proposed transfer on July 5, 1948, of the hospitals of Great Britain into the ownership of the State. The implications of this revolutionary step will become more and more visible as the months and the years pass. While many consultants and specialists may accept this as an inevitable step, and some may accept it as a desirable step, we believe that the majority are still opposed to a State Medical Service. In the last plebiscite more than 50% of consultants and specialists voting voted against negotiations with the Minister under the present Act. Consultants and specialists may now consider that if there is to be opposition to the State Medical Service foreshadowed in Mr. Aneurin Bevan's Act it must come, if it is to come, principally from general practitioners and that they as consultants and specialists will have little part to play. Those who observed the difference in Mr. Bevan's manner when he addressed himself to the Consultant section of the Negotiating Committee on Dec. 2 and 3 were left in no doubt that he hoped to rule by dividing. But if we fail, because of our differences, to preserve unity as a profession we shall lose what chance is left of moulding the Health Service according to professional ideals. Apart from all this the consultant may feel himself to be in a dilemma. Firmly opposed as he may be to a State Medical Service he knows that to work in a hospital is for him the supreme necessity of his professional life. What, he may well ask, will happen to him if he sees the hospital gates shut against him because of his refusal to work in the National Health Service under the terms of the present Act? This is a dilemma, but one which we believe to be of little significance between now and July 5, 1948. In the first place the report of the Spens Committee on the remuneration of consultants and specialists is unlikely to be completed before Easter. Once the report of this Committee is published it will have to be scrutinized carefully by the profession as a whole and by the various bodies which represent the consultant world. And when the professional debates on this Committee's report have come to an end there will be the inevitable negotiations with the Ministry of Health. These are not matters that can be settled

[1] *British Medical Journal Supplement*, 1939, 2, 231.
[2] Ibid., 1939, 2, 247.

quickly, because of the varying nature of the commitments consultants will have to undertake. It is therefore highly unlikely that consultants will be in a position to sign contracts of service before July 5, 1948, because for one thing the Government will not be in a position to offer them. They will continue their work in their own hospitals on the same basis as at present. To put it at its lowest, then, consultants and specialists should have no need to fear that by adhering to a principle they will endanger their careers or suffer financial loss. Again, if the result of the plebiscite is the same as the plebiscite of a year ago, no Minister of Health could prevent sick persons in hospitals from receiving the skilled services of such a large number of the consultants and specialists in this country.

The medical profession in Britain is now faced with the most important issue in the whole of its long history. We live in times when ideals and traditions are at a discount and when the cynic may too easily prove his case that principles may be dissolved in gold—or its many equivalents, of which power is one. Mr. Bevan has somewhat cynically dangled before the consultant the bait of no-ceiling paying beds in some State hospitals. But neither this nor his promise to exclude private nursing-homes from State control will affect those consultants—and we believe they are many—who see this Act as the first fulfilment of the Government's policy to introduce a whole-time salaried State Medical Service. This is the one central fact of the present deep conflict between the medical profession and the Minister of Health. He has refused to shift his ground and the profession must be equally resolute in refusing to shift its ground. We have a responsibility to the past as well as to the future, and we have a responsibility to the profession not only in this country but also in others. Unfortunately the World Medical Association at its meeting in September last year in Paris did not find time to hold the debate which all were anxiously awaiting—on the relationship between the doctor and the State. But in the intervals of the meeting, when medical men of close on fifty nations could discuss matters freely, this was clearly the one subject that was of the greatest concern. Medical men in the Dominions, in the U.S.A., in Scandinavia, in Europe, in India, in the Middle East, in China, are all sorely perplexed by the growing tendency of the State machine to thrust itself between the individual doctor and the individual patient. They see this intervention of the State as something essentially harmful to medicine, and they look to this country for a lead and are anxiously awaiting the outcome of the present struggle. The consultant and the general practitioner form an organic whole. Without the closest co-operation between these two the patient suffers. Both general practitioners and consultants must, therefore, resist the painfully obvious attempts being made to sever them. If those who are like-minded in their opposition to a State Medical Service stand firmly together they need remain in no doubt about the result. Mr. Bevan has the advantage that he has to make up only one mind. The medical profession is a collection of highly individualistic minds, but its problem is in essence simple, and that is to make its collective view clear on one point—whether or not it is in favour of a State Medical Service.

PENICILLIN IN BACTERIAL ENDOCARDITIS

It is surprising to recollect that until three years ago the treatment of subacute bacterial endocarditis with penicillin was strongly discountenanced in this country, the official attitude being that the large amount of the drug required could be better employed in other ways. This was perhaps true until that time, but sufferers from this disease have since been more fortunate. Encouraged by reports of its successful treatment in the U.S.A., and by the improving supply position, the Ministry of Health allocated a quantity of penicillin for this purpose at the beginning of 1945, and the control of its use was entrusted to a committee of the Medical Research Council. This committee established fourteen centres where the treatment could be carried out in accordance with a preconcerted plan, and results from all centres have been reported to the committee. A report on earlier results by the secretary of this committee, Prof. R. V. Christie, appeared in this *Journal*[1] early in 1946. We now publish (p. 1) a second report in his name amplifying the previous observations not only by the inclusion of further cases but by a more searching analysis of results which have gained in significance by the longer period of the follow-up. This is the largest series of such cases on record, and it makes plain the advantages of organizing the study of a new and difficult form of treatment as a piece of co-ordinated research on a nation-wide scale. Had each institution undertaking this treatment been an independent unit, formulating its own plans and having to base conclusions only on its own experience, a good deal would perhaps have remained uncertain which is now statistically well ascertained.

In the first series of findings it was made clear that the duration of treatment was all-important, and that when this was standardized at one month the larger the dose within the limits then employed the better the results. In the earlier report the numbers on which this conclusion was based were small, but much more extensive experience has been only confirmatory. Of 58 patients given 500,000 units daily, only 6.9% died with the infection uncontrolled or relapsed; among 83 patients given 250,000 units this proportion was 16%, and in 17 receiving only 100,000 units daily it was 41%. The superiority of the largest dose is thus clearly evident, and it may be expected to eliminate the infection in at least 9 cases out of 10. On the other hand, about 35% of these initially successful cases die of heart failure or other complications, and the over-all recovery rate is thus not likely to exceed 60%. That heart failure should figure so largely as a cause of death is perhaps not so unexpected as this report seems to suggest. Unless diagnosed very early, this disease causes a degree of valvular destruction and incompetence unequalled in any other condition, and there is no evidence that healing improves the function of the valve; fibrosis and calcification may even worsen it. Whatever the achievements of chemotherapy, some of these patients must always die from the mechanical consequences of damage done before the diagnosis is made.

From this analysis there are several conclusions which emerge clearly, and other features which remain to be

[1] 1946, 1, 381.

explained. Prognosis is affected by five factors, of which the duration of the disease, the presence or absence of heart failure, and the state of nutrition have the most decided effect. Since the two latter depend largely on the first, they may be regarded almost as different expressions of the same thing, but they lay treble emphasis on the paramount importance of early diagnosis. The vast majority of these patients owe their predisposition to past rheumatic carditis, and a history of this disease should be borne constantly in mind. If unexplained fever in such a patient were always regarded as demanding hospital admission forthwith and a series of blood cultures, very early diagnosis would be the rule and the recovery rate would undoubtedly improve. Prognosis depends also on age, but only clearly to the extent that it is worse in patients over 50. It also depends on the site of the lesion, combined aortic and mitral disease having the worst prognosis, and septal defects the best. There were only 12 cases of septal defect, and the figures are therefore not conclusive; but the absence of valvular damage puts this form of the disease in a different category, and it would be surprising if the ultimate results were not more favourable. It also seems that the prognosis is worsened by previous treatment with penicillin; the difference is decided if relapse has occurred after a full course, but less marked if previous treatment has been inadequate.

The features which remain to be explained are failure to control infection in a small proportion of patients adequately treated, and relapse—usually within a month—in others in whom treatment was initially successful. It has also been observed that in about one-third of the patients dying after apparently effective treatment "what appeared to be living organisms" were still present in the affected valves. It might have been supposed that the degree of susceptibility of the causative organism to penicillin would be an important factor here. This is known to vary widely, the growth of some of these streptococci being inhibited by less than 0.02 unit per ml.—the approximate concentration inhibiting that of the Oxford staphylococcus—while other strains require many times this amount. The influence of this factor has been analysed in all possible detail, and it seems that unless the coefficient of resistance is 8 or more it has no observable effect. Until the cause of this sort of failure is understood it is unfortunately by no means certain that the higher dosage it is proposed to use will have any better effect. It will be noted that this study is to be continued at eight of the centres which co-operated in the earlier work: they are named at the end of the report, with an invitation that cases be sent to them.

CONDITIONED VITAMIN-D DEFICIENCY

In most children freedom from rickets is ensured if the diet contains adequate and well-balanced amounts of calcium and phosphorus, and if vitamin D is supplied either in the food or by exposure of the body to sunlight. Older subjects are similarly protected from osteomalacia, the adult counterpart of rickets. In some instances, however, calcification is defective even with a diet which appears to be satisfactory, and therapy with ordinary doses of vitamin D is unsuccessful. Among these special patients some may have lesions beyond the control of vitamin D, but others may be cured by very heavy dosing. Thus ten years ago the American workers Albright, Butler, and Bloomberg[1] reported that a patient who had suffered from rickets for many years in spite of ordinary doses of vitamin D was cured when the dosage was raised to 450,000 i.u. daily. Subsequently Albright and his colleagues[2] described a series of cases in which osteomalacia was associated with steatorrhoea or with renal lesions. Some of these patients responded to massive doses of vitamin D and were considered therefore to have an abnormal resistance to the vitamin.

In this country R. A. McCance[3] has recently studied an interesting case in which severe osteomalacia was traced to R.R.D. (raised resistance to D). The patient, a young woman, came under his care about eight years after the start of her illness. Her early history had been uneventful; she had been born of healthy parents and developed into a strong schoolgirl with a good record in athletics. When she was 14 years old, however, her gait became abnormal. This symptom was soon followed by great muscular weakness, which made it difficult and painful for her to walk, or even rise from a sitting posture. Primary muscular dystrophy was diagnosed and was treated with glycine, but after a slight temporary improvement the patient's condition deteriorated during the next two years until she became completely crippled. *X*-ray examinations now revealed decalcification of the skeleton and deformity of the pelvis. Serum phosphorus was low, but calcium was normal. When the patient was aged 18½ years, therefore, a double diagnosis of myopathy combined with osteomalacia was entertained. If any further evidence of decalcification was necessary it was soon provided by spontaneous fractures of one ulna, the pelvic bones, and extreme coxa vara. Vitamin D was now given in doses of 2,000–7,500 i.u. daily. Some progress was made, and although decalcification persisted walking became possible with the aid of crutches.

When the patient was 23 years old she came under the observation of Prof. McCance. No evidence was found of abnormalities in her kidneys or intestinal tract. A careful study of her calcium and phosphorus metabolism was made, and the balance for both was found to be negative. *X*-ray examinations indicated the presence of spontaneous, idiopathic, symmetrical pseudo-fractures which were clearly identical with lesions which have been described by Looser[4] and Milkman.[5] In spite of a good dietary history, and of exposure to irradiation as indicated by a sunburnt skin, vitamin D therapy was instituted at the high level of 500,000 i.u. daily. No dramatic change was noticed during the first 14 days of dosing, but soon afterwards both calcium and phosphorus were found to be in positive balance. The faecal excretion of calcium fell to about one-tenth of the previous level, although an increased excretion by the kidneys reduced the net gain. With phosphorus the threshold value of excretion by the kidney appeared to be increased. After therapy had been kept up for about six weeks, with a total intake of 21,000,000 i.u. of vitamin D, there was some evidence of toxic effects, and dosing was stopped. The patient's condition, however, continued to improve. After four months, *x*-ray examination showed considerable recalcification, with callus formation at the sites of the pseudo-fractures. Ten months after treatment recalcification was still proceeding at the rate of 5 g. weekly, while the bones appeared almost normal on *x*-ray examination. The final state of the patient, one year after treatment, was most satisfactory. She had no

[1] *Amer. J. Dis. Child.*, 1937, **54**, 529.
[2] *Medicine*, 1946, **25**, 399.
[3] *Quart. J. Med.*, 1947, **16**, 33.
[4] *Dtsch. Z. Chir.*, 1920, **152**, 210; *Zbl. Chir.*, 1920, **47**, 1470.
[5] *Amer. J. Roentgen.*, 1934, **24**, 29.

pain, could walk with confidence, and was physically capable of earning her living. In addition to providing an illustrative and authentic example to add to our list of conditioned vitamin deficiencies, therefore, Prof. McCance has had the satisfaction of restoring to a normal life a patient who appeared to be a hopeless cripple.

CHOLERA IN EGYPT

The recent epidemic of cholera in Egypt began in September at El Kurein in the Delta province of Sharkiya. Details were given from week to week in our epidemiological notes, and some account of the measures taken to control the epidemic appeared in these columns.[1] It is now clear that during the first week the infection spread from Sharkiya to the neighbouring provinces of Dakahliya, Minufiya, and Kalyubiya in Lower Egypt, and to Ismailia and Suez. By the end of the second week there were cases in Upper Egypt, and all the Delta provinces were involved except Beheira. It was at the end of the fourth week that the curve of incidence rose steeply to the peak figure of 1,022 cases, with 581 deaths, on Oct. 20. In that week there were 4,566 cases, with 2,057 deaths.

The later course of the epidemic has recently been reviewed.[2] The worst day was Oct. 20, but the fifth week brought a further 5,976 cases and 2,933 deaths, and by this time 367 of the 425 villages in Dakahliya Province were affected. A decline began in the sixth week and thereafter continued steadily. During the eighth week no new areas were affected, and in the seven days there were reported 750 cases and 505 deaths. Over the eight full weeks from Sept. 23 to Nov. 16 there was a total of 20,877 cases, with 10,265 deaths—a case fatality of 49%. It should perhaps be recalled that when Egypt experienced its last cholera epidemic forty-five years ago there were over 40,000 cases, with a case fatality rate of 85%, and since the 1902 epidemic the population of Egypt has almost doubled. Once again the great majority of the cases appeared in the villages, and the disease failed to establish itself in any of the towns provided with satisfactory water supplies and adequate sewage disposal systems. It is true that the over-all incidence began to decline as soon as 80% of the population had been inoculated with anti-cholera vaccine, but whether this represents a causal relationship or merely the coincidence of inoculation and a spontaneous autumnal decline it is too early to say.

The part played by the World Health Organization in meeting a grave threat to international public health augurs well for the future. As soon as news of the outbreak was received members of the Interim Commission were consulted and authorized certain expenditure. The Division of Epidemiology advised all countries connected with Egypt by land, sea, and air routes, and every country which might possibly be concerned was provided with up-to-date information and thus enabled to take the necessary quarantine measures. The expert committee on quarantine met in Geneva, and we reported then the measures that were advised or that had already been taken by the Egyptian Government.[3] So far as this country is concerned, only one individual arriving by air from Egypt was ever suspected as a possible case of cholera,[4] and this suspicion proved to be unfounded. It should also be recorded that the mere concentration of orders for cholera vaccine through the W.H.O. Secretariat is said to have resulted in a saving for the Egyptian Government of $125,000.

[1] *British Medical Journal*, 1947, **2**, 619.
[2] *Chronicle of W.H.O.*, 1947, **1**, 157.
[3] *British Medical Journal*, 1947, **2**, 801.
[4] Ibid., 1947, **2**, 851.

HABITUATION TO STREPTOMYCIN

Bacteria can acquire some degree of tolerance to almost any lethal agent. Unfortunately the antibiotics are far from being an exception to this: penicillin-resistant strains of certain species, particularly *Staph. aureus*, are now frequently encountered, and this subject was discussed in a leading article in the *Journal* of Nov. 29. But no such habituation as that exhibited by some bacteria on contact with streptomycin has ever been seen before; it is well recognized as a defect which severely limits the usefulness of this drug and renders its employment always something of a gamble. How rapid and extreme the change may be is illustrated in the studies of Finland and his colleagues[1] of the treatment of urinary tract infections caused by coliform bacilli. These organisms, originally inhibited by not more than 25 units of streptomycin per ml., became resistant within a few days—in one patient after only one day—to no less than 50,000 units per ml. Similar observations are features of many reports of failure in streptomycin treatment for conditions of various kinds. There has been much speculation about the mechanism by which this resistance is acquired, and some authors believe that the original bacterial population may contain a very small minority of naturally resistant cells. Alexander and Leidy[2] offer actual proof of this, obtained by the study of cultures of *H. influenzae* from cases of meningitis. By inoculating with enormous numbers of organisms media containing 1,000 units of streptomycin per ml. they obtained a few colonies, thus indicating that an infinitesimal proportion (1 in some billions) of cells in cultures obtained before treatment was begun possessed this high resistance. Strains from 14 patients all behaved in this way *in vitro*, although 10 of the patients had been cured by streptomycin and 4 had not, failure in 3 being attributable to the development of resistance *in vivo*. These authors believe that the outcome of treatment depends on whether one or more of these resistant cells is present when treatment is begun. The probability of this increases with progress of the disease and the greater total number of bacilli in the meninges. A patient whose strain developed resistance during treatment was found to have in the nasopharynx a year later *H. influenzae* still resistant to 1,000 units of streptomycin per ml. It is clearly only a matter of time before such strains become common, if not predominant, and a new antibiotic will consequently be needed.

A stage further than habituation has now been described, no less than the ludicrous situation in which a previously susceptible organism now requires streptomycin to enable it to grow and produce disease. Miller and Bohnhoff[3] have shown previously that meningococci originally very susceptible to streptomycin can be trained within a week to withstand 75,000 units per ml. In an extension of these studies[4] they have observed two types of resistant variant. One of these is unchanged except in its capacity for resistance to the drug; it grows normally on all media, whether containing streptomycin or not, and retains its previous pathogenicity for mice. The second type grows only on streptomycin-containing media, having lost its capacity for growth on ordinary media altogether. Its behaviour in mice corresponds: avirulent in the ordinary sense, it assumes full virulence, producing a fatal infection, only in animals treated with streptomycin. What are we to think of a chemotherapeutic agent which can become an essential growth factor for a previously susceptible organism?

[1] *J. Amer. med. Ass.*, 1946, **132**, 16.
[2] *J. exp. Med.*, 1947, **85**, 329, 607.
[3] *J. Amer. med. Ass.*, 1946, **130**, 485.
[4] *Science*, 1947, **105**, 620.

PULMONARY HEART DISEASE

Pulmonary heart disease may be defined as a disorder of the heart resulting from disease of the lungs or of the pulmonary circulation. It may be acute, as in massive pulmonary embolism ; subacute, as in recurrent thrombo-embolism and secondary carcinomatosis of the lungs ; or chronic.

Massive pulmonary embolism is responsible for approximately 1% of all obstetrical, surgical, and medical deaths in hospital. Thrombosis usually begins in the calves of the legs. The most useful early sign of a dangerous phlebothrombosis is a rise of the skin temperature of the affected leg. The clinical features of massive pulmonary embolism include sudden faintness and dyspnoea, substernal constricting pain, an abrupt and marked fall of blood pressure, elevation of the venous pressure, and signs of profound compensatory peripheral vaso-constriction. The most certain way of making a correct diagnosis is by means of multiple chest-lead electrocardiography.[1] Treatment by heparin and dicoumarol should be instituted at once, preferably as soon as phlebothrombosis is suspected.

An interesting form of pulmonary heart disease is that due to progressive blocking of the pulmonary circulation by carcinomatous emboli or by multiple thromboses secondary to perivascular lymphatic carcinomatous infiltration.[2] Chorion-epithelioma or carcinoma of the stomach is usually responsible.

Chronic pulmonary heart disease is of two main types, hypertensive and anoxic, though the latter rarely, if ever, occurs alone. Hypertensive pulmonary heart disease may be of known or unknown aetiology. Known causes include bilharzia, periarteritis, and Buerger's disease, but the majority of cases seen in this country are of obscure origin. The sexes are equally represented. Most of the patients reported have been relatively young, and some have been children. Clinically, the disease is characterized by a preliminary variable period of breathlessness, followed by progressive congestive heart failure with a high right-ventricular pressure, low cardiac output, normal or near-normal arterial oxygen saturation, and peripheral cyanosis. There is radiological and electrocardiographic evidence of great enlargement of the right ventricle, and the pulmonary artery is dilated. Treatment is singularly ineffective and the outcome invariably fatal.

Pathological findings have been variable. Medial hypertrophy of the smaller arteries is far from constant, and when present rarely affects more than about a quarter of the vessels.[3] Intimal thickening of patchy distribution is the rule, and atherosclerosis is commonly extensive. Multiple thromboses have also been described and, when old, may be difficult to distinguish from atherosclerotic lesions. Dilatation of the pulmonary artery may be associated with medial hypoplasia, as in the case described by Gold.[4] Gilmour and Evans[5] reported a case very similar to Gold's, and suggested that endarteritis, which seemed to be responsible for the hypertension, began as a compensatory reaction to medial hypoplasia. They thought that a vicious circle then became established, endarteritis leading to hypertension and hypertension to further endarteritis. As the authors observe, however, medial deficiencies are not believed to be the rule in cases of " primary pulmonary vascular sclerosis." Nevertheless, the idea that some congenital abnormality of the pulmonary arterial tree may be an important aetiological factor in these cases is worth further investigation.

The anoxic type of pulmonary heart disease is characterized by a long history of chronic bronchitis or asthma, evidence of marked emphysema, cyanosis due to reduction of the arterial oxygen saturation, compensatory elevation of the cardiac output,[6] and finally by congestive heart failure. The right ventricular pressure is raised,[7] but much less so than in " primary " hypertensive cases. *X*-ray investigation again shows enlargement of the right ventricle and dilatation of the pulmonary artery. It is possible that anoxia due to emphysema is responsible for the hypertension.[8] Aneurysmal dilatation of the pulmonary artery, of its left or right branch, or of all three may occur when medial hypoplasia is associated with pulmonary hypertension from any cause.

[1] Wood, P., *Brit. Heart J.*, 1941, **3**, 21.
[2] Brill, I. C., and Robertson, T. D., *Arch. Intern. Med.*, 1937, **60**, 1043.
[3] Brenner, O., Ibid., Parts 1–4, **56**, 211, 457, 724, 976.
[4] Ibid., 1946, **78**, 197.
[5] *J. Path. Bact.*, 1946, **58**, 687.
[6] Howarth, S., *et al.*, *Clin. Science*, 1947, **6**, 187.
[7] Cournand, A., *et al.*, *J. clin. Invest.*, 1946, **25**, 639.
[8] Motley, H. L., Cournand, A., Werko, L., Himmelstein, A., and Dresdale, D., *Amer. J. Physiol.*, 1947, **150**, 315.

INTRATHORACIC NEUROGENIC TUMOURS

Neoplasms arising from nervous tissue are the commonest tumours of the posterior mediastinum. They grow from the sympathetic system or from an intercostal nerve and originate from Schwann cells, connective-tissue cells, or true nervous tissue. Most of them are benign but some are malignant, or become malignant after many years. Even those that are not biologically malignant threaten life, like all intrathoracic tumours, owing to their position ; they may grow rapidly and become very large. Although these tumours are comparatively rare, they are being met with in larger numbers to-day because of the increasing applications of radiography. Susman[1] describes four cases treated by operation ; two were examples of sympathetic ganglio-neuromata, and two were neurofibromata arising from the sheath of an intercostal nerve. One of these last appeared in a child aged 11 who had a generalized neurofibromatosis —von Recklinghausen's disease. A huge left basal tumour eroding two ribs was removed, but several months later complete paraplegia developed and death followed. This liability of the neurogenic tumours to be associated with an intraspinal portion (dumb-bell tumour) is another reason for operative removal.

Olivier Monod,[2] in a study of 19 cases, states that it is better not to attempt removal, unless there is definite compression, when the tumour is a part of a neurofibromatosis because of the danger of malignant change. He points out that the neurogenic tumours are usually solitary, rounded, posterior, and subpleural ; they have a poor blood supply and are easily freed and removed. Symptoms are often slight and the differential diagnosis must generally be made radiologically and depends upon the demonstration that the tumour is in the posterior mediastinum. Artificial pneumothorax often helps diagnosis by dissociating the lung from the tumour. Any pulmonary symptoms such as cough or haemoptysis are against the diagnosis of a neurogenic tumour. Monod recommends extrapleural rather than transpleural removal. Of the 17 tumours that he has removed, 11 were dealt with extrapleurally. His description of the extrapleural approach is interesting and should be consulted, but it is not entirely satisfactory except for the smaller tumours. It can be seen from his radiographs that it has been necessary to resect as many as four ribs. A transpleural approach should enable even a very large tumour to be removed after resecting only one rib, with possibly the division of one adjacent rib. Most thoracic surgeons feel that it is difficult to avoid opening the pleura when removing a large tumour, and the extrapleural approach is so apt to be cramped that they prefer a deliberate transpleural operation for almost all cases.

[1] *Austral. New Zeal. J. Surg.*, 1947, **16**, 200.
[2] *Le Poumon*, 1947, **3**, 97.

CANCER RESEARCH

ANNUAL REPORT OF B.E.C.C.

The Annual Report of the British Empire Cancer Campaign consists as usual of a compilation of separate reports from research laboratories, radium institutes, and hospitals, as well as from individual investigators, scattered over this country and to some extent over the Dominions. Most of the chemical, physical, and biological investigation here recorded is of a highly specialist character, employing techniques familiar only to those working in that particular field. For the twenty-fourth year in succession Mr. J. P. Lockhart-Mummery has done a useful service in editing this mass of material, but even so it is not easy to place all this work in perspective. As Lord Horder put it at the annual meeting of the Campaign recently, many pieces of the jig-saw have been found, but the master-piece which reveals the picture is still hidden. Many of the investigations which are proceeding are long-term ones, and immediate results are not to be expected. Among the investigations described are those on the production of gene mutation in mice by dibenzanthracene, the cytochemistry of avian tumours, and the effect of sulphamezathine in inducing precocious growth in young cockerels. Every ray of light, however indirect, is presumably valuable, and one of the fascinating things about work of this kind is that no one knows at what point the whole landscape may be suddenly illuminated.

Mass Statistics

In the present report an unusually large number of cancer statistics is given. At a recent symposium on breast cancer at the Royal Society of Medicine the main controversy appeared to surround not competing methods of treatment but the interpretation to be placed upon statistics. Statistics, it is said, can be made to prove anything—even the truth. At this symposium three-year survival rates were discarded altogether. Even five-year rates were looked upon in some quarters with scepticism, and one speaker argued that the percentage claimed by one surgeon as his ten-year survival rate after operation was in excess of the ten-year expectation of life for the normal population of the same age group, demonstrating to his mind the fallacy underlying all statistics on such bases.

Whatever their exact worth, however, such statistics as are quoted in this report are of interest. The Marie Curie Hospital, for example, records 1,832 cases of cancer of the cervix treated radiologically, mostly by radium alone, since 1925. The five-year survival rate here for all the four stages is given as 45%. Attention is drawn to the difficulty of estimating the relative merits of surgery and of radiology in cancer of the body of the uterus, because comparable groups of cases treated primarily by either method are not easy to obtain. The same hospital has treated 510 cases of breast cancer over a period of 25 years, and gives the ten-year survival rate for patients in stage I as 27.2%, and for stage II, 17.6%.

Cancer of the Lung

Under the leadership of Sir John Kennaway workers in the pathological department at St. Bartholomew's Hospital have been studying the death certificates for cancer of the lung and of the larynx in men during the period 1921–38. During this period deaths attributed to cancer of the lung increased by 16.5 times in men, and by 8 times in women, though the incidence of cancer of the larynx has not risen in either sex during the last fifteen years. The examination of occupations does not disclose anything which would account for a large fraction of the increase in these deaths, and the two largest industries in the country, agriculture and coal mining, show a low incidence. The possibility of the great increase in the habit of tobacco smoking being a factor has been considered. During the period in question the consumption of tobacco roughly doubled. But the investigators do not commit themselves on this or any other factor in causation, nor indeed on whether or to what extent the increase is a real one.

The Clinical Cancer Research Committee of the Campaign presents every year a highly elaborate statistical analysis of cases of cancer, derived from London hospitals, pertaining to some region of the body. This year attention is given to 916 cases of cancer of the colon and the results are analysed in some 40 tables. Cancer of the caecum and proximal colon is relatively more common among females, who form 60% of the cases. In cancer of the descending colon and sigmoid the proportion of the sexes is nearly equal. The mean ages of males and females in this series were 62.1 and 60.8, respectively. No significant variation was found pointing to an occupational factor among the males. The patients who consulted a doctor within three months of the onset of symptoms constituted 63% of the whole series. In 21% palliative treatment had been persisted in for more than three months before reference to a hospital. Radical operation was possible in only a little over one-third of the cases, with a mortality of 18.3%. The five-year survival rate was 31.2%.

Of the various radiobiological investigations which are recorded attention may be drawn to some interesting work carried out in the department of biophysics at Mount Vernon, which was lately brought before the British Institute of Radiology. This concerns the effect of ionizing radiations on the broad-bean root (*Vicia faba*). These roots have been found to be more easily damaged by *x* rays when irradiated either at 3° C. or when under the influence of hydrocyanic acid, and less easily damaged when irradiated in an atmosphere of nitrogen. The difference between the degree of growth inhibition resulting from aerobic and anaerobic radiation has been shown to be closely related to the difference in the proportion of cells in which structural changes in the chromosomes are produced under corresponding conditions of radiation.

Virus Research

The Campaign awarded some £75,000 as grants to hospitals and research workers during the year, and made a further special grant of £25,000 for virus research in relation to cancer. This special grant is to be applied over a period under the direction of the Scientific Advisory Committee. Work has been begun under its auspices in Glasgow, at the Royal Cancer Hospital; in Edinburgh, at the Institute of Animal Genetics; and in London, at the Middlesex, Royal Cancer, and Westminster Hospitals. The scheme embraces all aspects of the problem, including the use of the electron microscope and of the ultra-centrifuge, and an important part of the project is the training of workers in virus research. It takes from six months to two years for even a bacteriologist, if his previous studies have been limited to bacteria, to master the finer manipulations required in virus work. It is expected that the £25,000 will need to be considerably supplemented as the work goes on.

On the whole of this slow-moving and many-sided research Lord Horder's speech at the annual meeting may again be quoted: "We can juggle (I use the word deliberately) with carcinogens, with oestrogens, with susceptible and with resistant animal strains, with invisible 'agents' and with undefined 'factors,' but the essential causation of cancer in a woman's breast or in a man's stomach still eludes us."

Reports of Societies

RENAL FUNCTION IN DISEASE

At a meeting of the Manchester Medical Society on Dec. 3 Prof. ROBERT PLATT gave an address on "Renal Function in Disease."

He first considered the syndrome of renal failure, which was characterized by a steady deterioration in the power of the kidney to produce a concentrated urine; in the later stages the urine was pale, copious, dilute, and had a specific gravity of about 1010. When the functional power of the kidney was insufficient for the excretory needs of the body the symptoms of uraemia developed, not only because of retention of the waste products of metabolism but because of a general

disturbance of such electrolytes as sodium, potassium, chloride, calcium, and phosphates. The symptoms of uraemia—weakness, anaemia, anorexia, vomiting, wasting, drowsiness, and coma—should be clearly distinguished from the more dramatic symptoms of hypertension, such as severe periodic headache, retinal disturbances, convulsions, and paralyses, which so often co-existed and confused the clinical picture.

The first question to be discussed was why the kidney lost its concentrating power in renal failure. The underlying pathology common to all cases was loss of nephrons, and the usual explanation of the lack of concentrating power was that there was a failure of the cells of the tubules to continue their function of elaborating a highly differentiated urine. This theory was unsatisfactory. Rose Bradford showed fifty years ago that surgical removal of most of the kidney caused the remainder to secrete urine of the same type—copious, dilute, and of low specific gravity. It was inconceivable that in the circumstances the remaining nephrons should suddenly have developed tubular failure. Verney and Winton showed many years ago that an increase in glomerular pressure would also give rise to a urine of this type. More recent investigations by means of inulin and diodrast clearances had shown that the filtration fraction in chronic renal disease was high, which suggested that there was in fact a high glomerular pressure. If this was so, he suggested that it might be brought about simply by a large amount of blood perfusing a small number of nephrons. There could be no humoral mechanism involved because it was possible to have a condition of renal failure in one kidney while the other kidney was secreting a normally concentrated urine.

If it were accepted that a high glomerular pressure accounted for the character of the urine in renal failure, this did not rule out the possibility of a co-existing tubular failure in some cases, but failure of the tubule cells should give rise to glycosuria—which was never present in chronic renal disease. Moreover, the histology of chronic nephritis showed in general that in those areas where there was tubular atrophy the glomeruli were non-functioning, whereas the few remaining glomeruli were surrounded by apparently active and dilated tubules.

Prof. Platt then considered the question of oedema in acute nephritis. This was not due to hypoproteinaemia nor to heart failure. Current literature still subscribed to the view that it was due to increased capillary permeability. This view, which was never satisfactory, was based on observations on the protein content of the oedema fluid in acute nephritis which had since been discredited. Prof. Platt suggested that a low glomerular pressure would account for the scanty urine of high specific gravity which was typical of the early stage of acute nephritis, and would lead to increased reabsorption in the tubules, giving rise to fluid retention and oedema. Inulin and diodrast clearances supported this hypothesis by showing a low filtration fraction. Recent work in Manchester and elsewhere suggested that there was haemodilution with a high blood volume in the early stages of acute nephritis, a finding which supported the view that the kidney was primarily at fault and was strong evidence against the theory of capillary permeability.

Finally, Prof. Platt described briefly the recent work of Trueta, Barclay, and others, which had shown that the renal circulation could be largely diverted from the cortex into the medulla, and he discussed the bearing of these researches on reflex anuria and cortical necrosis of the kidney.

Drs. MARSDEN, ISRAELS, R. W. FAIRBROTHER, LANGLEY, DON, OLIVER, and Prof. G. JEFFERSON, F.R.S., took part in the subsequent discussion, to which Prof. Robert Platt replied.

PRIMARY STERILITY

At a meeting of the Section of Obstetrics of the Royal Academy of Medicine in Ireland, held in the Royal College of Physicians of Ireland on Nov. 7, Dr. BETHEL SOLOMONS took the chair in the absence of the new president, Dr. O'Donel Browne, who was recently elected Master of the Rotunda.

Dr. RAYMOND G. CROSS presented a series of 358 cases of primary sterility which had been investigated and treated at the Rotunda Hospital by Dr. A. H. Davidson during the years 1935–9. He found the causes of female sterility in his series to be as follows:

	No. of Cases	Percentage of Total
Fibroids	37	10.3
Ovarian cysts	26	7.2
Retroversion	81	22.6
Endometriosis	7	1.9
Tuberculosis (genital)	12	3.3
Adhesions	39	10.8
Salpingitis (unilateral)	27	7.5
Salpingitis (bilateral)	13	3.6
Hypoplasia	26	7.2
Anovular menstruation	8 in 136	5.8
Gonococcal infection	3	0.8
Uterus bicornuata	1	0.27
Carcinoma	1	0.27

A postal survey was carried out to determine the number of patients who subsequently became pregnant; 211 patients replied, and 81 had become pregnant. This represented 38% of the known results and 23% of the total cases. He analysed in detail the pregnancies in the various conditions and compared and contrasted them with the figures from centres in Europe and America. He emphasized the good prognosis in fibroids, ovarian cysts, endometriosis, non-tuberculous salpingitis, and adhesions due to appendicitis. He further discussed the investigation and treatment of hypoplasia and anovular menstruation, and finally drew attention to the poor prognosis in cases of genital tuberculosis.

Dr. BETHEL SOLOMONS asked what was the interval which elapsed before a marriage was considered sterile? One and a half years was a fair average. Although this inquiry was into female sterility, the results were incomplete unless the number of males responsible was shown; in his clinic the male was responsible in 50% of cases. The removal of fibroids meant a cure in a large number of cases, but it should be followed by insufflation of the tubes if pregnancy did not occur within six months. While pregnancy could occur when the uterus was in retroflexion, if the marriage remained sterile and this displacement was present it should be corrected. The removal of an ovarian cyst was also followed by increased fertility. Although the results of salpingostomy were disappointing, pregnancy occurred after a skilfully performed operation in 8 to 10% of cases. Tuberculosis of the Fallopian tubes was difficult to diagnose even when the abdomen was opened. If the tubes were tuberculous, the outlook for pregnancy was hopeless. When the condition was diagnosed, ultra-short-wave therapy was indicated rather than operation. Gonadotrophic hormones were valuable and should be used. The injection of a radio-opaque substance was strongly advised. He had done hundreds of salpingographies without any fatal results and with a minimum of complications. The injection of air, oxygen, or carbon dioxide had been followed by fatal results in several cases in Dublin. He had come to the conclusion that these fatalities were due to an absence of care in technique. Carbon dioxide should be used, the gas should be allowed to percolate very slowly, the pressure should be kept low, and no anaesthetic should be used.

General Discussion

Dr. A. W. SPAIN said that in dealing with these cases it was difficult to lay down any arbitrary time. In the younger group he would be inclined to wait for three years: in older women something should be done in a much shorter time. Curettage was helpful in the diagnosis of tuberculous salpingitis but should not be undertaken in the pre-menstrual stage.

Dr. J. GALLAGHER said that he did not regard as sterile any woman under 35 years of age until after at least three years of unfertile marriage. If the patient was over 35 years of age and had been married for one or one and a half years he would advise salpingography. Most cases in the "early married group" if left alone would become pregnant anyway. He did not think retroversion was a cause of sterility at all. Rubin's test carried a definite risk, and he knew of eight deaths following this investigation.

Dr. EDWARD SOLOMONS, Dr. E. A. KEELAN, Dr. F. GEOGHEGAN, and Mr. O'NEILL also joined in the discussion, to which Dr. Cross replied.

Correspondence

National Health Service

SIR,—The *Journal* of Dec. 20, 1947, makes a reference (p. 1005) to the premature disclosure in the *Tribune*, Dec. 12, 1947, of the discussions conducted by the Minister of Health with the Negotiating Committee. In an answer in *Hansard* (Dec. 19, 1947) the Minister declared that as far as he and his colleague, the Secretary of State for Scotland, and their respective officers are concerned he "could state categorically that no disclosure of any kind had been made or condoned of the discussions, which it had been agreed with the Negotiating Committee would not be published before Dec. 19, 1947." The *Tribune* notoriously draws its inspiration from leading members of the Socialist Party. Mr. Bevan's wife is a director, and he himself was closely associated with its management up to the time of his appointment as Minister of Health.

In these circumstances I submit that it is of the first importance that the profession should be made aware of the terms of this disclosure, and I would suggest further that the *Journal* should reproduce the full text. I would emphasize particularly the passages in which the *Tribune* editorial gleefully records and in great detail how the Minister rejected all the principal demands voiced by the medical representatives, adding the dubious information that "the Minister was supported in doing so by those negotiators who were not tied to the B.M.A." The editorial accords this final meed of praise: "Politically, the Minister's firmness has been most important . . . if he had been weak in face of this reactionary profession, it would have increased doubts as to the intention to carry out a Socialist programme."

In this connexion it must be emphasized that the official "Socialist programme," published in 1943, demanded the establishment of a full-time salaried State medical service, and Mr. Arthur Greenwood (then Lord Privy Seal) in the debate on the Second Reading (*Hansard*, May 1, 1946) stated quite firmly that that demand remains the party's ultimate and unalterable aim. It must be further emphasized that the "regulation-making power," reserved to the Minister in a measure hitherto unprecedented, would enable him to impose *by regulation* a full-time salaried State medical service when, as he foreshadowed in a speech in the House, "the time is ripe" to do so.

The *Tribune* further reports: "Aneurin Bevan made it quite clear to the Negotiating Committee that the service will start on July 5 'with the resources at our disposal.'" This repeats textually his reply to my question (*Hansard*, Nov. 10, 1947) in which I asked him to inform the House how many general practitioners and specialists he would require to warrant inaugurating the new health services and what measures had been taken to provide the buildings essential to carry out the undertakings of the Act. He evaded these queries with an answer which recalls a similarly defiant declaration made by the then Minister of Education in a public speech (February, 1946) that "the school-leaving age would be raised on April 1, 1947, *whether or not the teachers or the classrooms were there.*" It would seem that the Minister of Health is similarly resolved to "launch" the National Health Service Act, 1946, whether or not the doctors or the buildings are there. In these examples both Ministers are clearly more concerned with "carrying out a Socialist programme" than with effecting any real improvement in the existing provision of education and health services. In these circumstances, I submit, the profession will be indeed mad (*quem Deus vult perdere primum dementat*) if it hands to the Minister a blank cheque for him to fill in as he will, for that is what acceptance of the present Act would in effect mean.—I am, etc.,

House of Commons. E. GRAHAM-LITTLE.

SIR,—When doctors make partnership agreements or draw up a lease they employ experts to study the details and advise them. There are usually some clauses that the experts regard as important the importance of which escapes the non-expert. We do not hesitate to take the expert advice. I imagine there are thousands of doctors like myself who have neither the time nor the ability thoroughly to digest and understand the National Health Service Act. The Negotiating Committee has spent a very long time digesting and discussing all the clauses of this Act. It has looked into the obvious, the not so obvious, and the frankly obscure implications of each clause.

Certain principles are considered vitally important. Do not let us be fooled by plausible statements to the effect that the Negotiating Committee is making mountains out of molehills. Let us believe our own experts, who have studied the whole matter with so much care. Let us rally round and support the Negotiating Committee. Let us unite as never before, promise in writing not to join the Service until advised to do so by the Negotiating Committee, and stick to it. By so doing we shall not harm the Service but will safeguard the future, immediate and remote. Surely it is the remote future which is in so much danger.—I am, etc.,

Bungay, Suffolk. P. G. LEVICK.

SIR,—I am overwhelmed by the benevolence and thought for our welfare shown by that enemy of the upper and middle classes, Mr. Bevan. His attractive financial terms, his previous promises, and the exhibition of skilful skating over legally doubtful ice make delightful reading—almost a Christmas carol. But we must remember: (1) It is established that no Minister of the Crown is bound by his predecessors' promises. (2) Once we have sold our practices we have no legal say in what the purchaser does with them, and will lose all power of individual initiative.

We shall be dependent on a majority agreeing with our individual dislikes and the use of that loathsome weapon, a strike. In the meantime the basic salary can be raised at someone's discretion with a lowering of the capitation fee to balance, or just as likely, in view of an "imminent crisis," merely the latter; and we shall not be able to do a thing about it. Let us, therefore, set our faces against this modern search for easy flesh-pots and keep the standard of individual initiative flying for the rest of our great country to follow.—I am, etc.,

Cromer, Norfolk. A. H. GREGSON.

SIR,—I am strongly opposed to the National Health Service Act but am not greatly impressed by the Negotiating Committee's case, although the Minister has avoided answering any of the main points. Why does he insist on a basic salary when a system of Government grants for young practitioners would meet all reasonable difficulties?

I feel that I could influence my neighbours and partners if I had information on the following points: (1) Are salary and capitation fee subject to "regulation" by the Minister? (2) In actual fact how far are regulations subject to the control of Parliament? I understand that the Minister, in practice, has an almost free hand. (3) This Act is the work of one man. Therefore it is right for us to learn what we can of his character and political history before we decide to accept his word, which is what he naively asks us to do. What is his record? This is business, not a tea party.

I have a son of 16 who wants to go into general practice; my father too was a G.P. and my grandfather. Why I ask the above three questions is because I find my doctor friends drawn away from consideration of principles to the Minister's statement about remuneration. If these promises are to be mere scraps of paper we shall be forced to consider the main structure of the Act—to what extent we will agree to be his servants, with no alternative employment or employer.—I am, etc.,

Havant, Hants. M. S. DEWHURST.

SIR,—With the publication of the Minister of Health's reply to the Negotiating Committee, there is certain to be a spate of letters, discussions, and meetings on the subjects raised. May I suggest that much time and energy would be saved if members of the profession would realize that by the Minister's refusal to compromise on the seven basic principles laid down by the B.M.A. the position is entirely unchanged from the time when the plebiscite was answered by the profession earlier in the year?

It was then our feeling that terms of service could not usefully be discussed unless vital principles were conceded. As nothing has happened since then to modify the Minister's original attitude to our demands, it seems to me that Divisions and members should be warned against dissipating their efforts by discussing terms of service in a scheme which is patently unacceptable, as the liberties of the profession have not been safeguarded. Do we still hold to all we said and wrote in those days, or have we allowed ourselves to be "softened up" by the passage of time?—I am, etc.,

Tiverton, Devon. THOMAS N. RUDD.

SIR,—Why another plebiscite? Did not the profession indicate in the last its opposition to discussion with the Minister? Why should we allow ourselves to be added to the multitude of slaves of the State? Why present the Minister with our capital, the fruits of our labours? Why even discuss a medical service which fosters numbers and not quality?—I am, etc.,

Gerrards Cross, Bucks. H. N. HORNIBROOK.

SIR,—It is essential that the impending plebiscite on the Health Act should provide clear information not only of the views of members of the profession but also of the action they are prepared to take in support. There are many who dislike the Act but fear to vote against acceptance on financial grounds and others who would be content to accept it but not against the will of the majority of the profession. The former must be reassured and the numbers of the latter assessed.

I therefore suggest that two questions be asked: (1) Are you in favour of the profession accepting service under the Act? (2) Are you prepared to support the decision of the majority?

The decision should be taken on the vote of private practitioners only (consultant and general), whose future is at stake. Permanent officers of the Armed Forces, salaried officials of the Ministries, county councils, and other public bodies will naturally continue their work in any event, and their votes should not influence the issue.—I am, etc.,

Finchampstead, Berks. E. BILLING.

SIR,—The time has come when it is necessary to warn all those members of the medical profession who are inclined to regard any promise given by a Minister at the present time as necessarily permanent in the future. After a few years, when the profession is firmly in the grip of the Ministry of Health, the following can and most probably will happen: (*a*) On grounds of economy the remuneration of the doctors can be reduced, possibly without arbitration. (*b*) Private practice will ultimately dwindle, and it may happen that the Minister will issue an Order which will prohibit State medical practitioners from taking private patients. This could very well occur when the health centres are finally in operation. (*c*) Orders can be issued directing a doctor how he may or may not treat his patients, and he will have no more freedom or personal initiative than any other Civil Servant.

We have not forgotten that some years ago a Minister did in fact alter the terms of service, without consulting the profession, in spite of promises given beforehand. Also, we have learnt that an undertaking given by one Minister is not necessarily binding on his successors. Let us ponder these facts very carefully before we barter our heritage of freedom for a mess of pottage, however well sweetened.—I am, etc.,

Keighley, Yorks. B. A. SLOCOMBE.

SIR,—It is rather difficult, after several years of controversy about the National Health Service Act, to see the wood rather than the trees, but is it not at the back of all our minds that this scheme is as unrealistic as prohibition in America? The ordinary middle-aged doctor who has been any good at his job finds himself with an increasing reputation and demand for his services. He has always been able to meet this situation in one of two ways. If he is as strong as a horse, he can accept more and more patients. If not, he can raise his fees and so keep his work within the limits of his sclerotic arteries. That is the true reason why we fear to see the last of private practice: it reduces the incidence of coronary thrombosis in the medical profession.

As long as a sufficient part of the populace can pay fees, a doctor's life is endurable. A 100% service, whether salaried or by capitation fee, removes any possibility of self-protection except through the bankruptcy court. It puts a premium on untutored youth and physical stamina, and a discount on greying hairs and wise judgment. It is thoroughly bad and, if introduced, is liable to suffer the same fate as prohibition.—I am, etc.,

Ashtead, Surrey. W. EDWARDS.

SIR,—The Minister's reply was more conciliatory than some of us were led to expect. But paragraph 25, "The Doctor's House," requires explanation. Why did the Minister seek advice about the citizen's right inherent in the Common Law of the land to sell what he owns, and from what will the certificate of the Medical Practices Committee protect him? Surely this unnecessary information is there to confuse or to hide something.—I am, etc.,

Haddenham, Bucks. T. W. S. PATERSON.

SIR,—The Negotiating Committee's case and the Minister's reply show how far we have travelled already towards first the twilight and then the night of our freedom. Gild it how he may, the Minister is asking us to become Civil Servants, shackled to a State machine, ready to obey the rules and regulations made for us by him and his successors at the Ministry of Health.

It was in May, 1946, that the Representative Body of the B.M.A. passed a resolution by 210 votes to 29 rejecting State ownership of hospitals; and another by 214 votes to 2 rejecting control over doctors with regard to the area in which they practise. In summing up the results of this meeting, the Chairman commented: "Now we have come to the time when one side or the other has to give way. A conflict is inevitable." They were fine motions, fine words, but during the eighteen months that have passed since that date, by subtle whispering propaganda and clever parliamentary tactics, the Minister has been enabled to take action so that he has made the State ownership of hospitals inevitable. During the same period he has formed committees within the framework of the Act and found medical personnel to serve on them; and among other things the functions of these committees have very much to do with the control of doctors in the area in which they practise.

The Minister is a clever psychologist, and in many respects he has jockeyed the profession into false positions. Let us remember that all his premises are based on his false assumption that the working of the Act is inevitable. Let us not make the same assumption: once we do so, we are lost. Most of us are non-political and thoughtful members of society. We are convinced in our hearts, by the tradition we inherit, that the practice of medicine must remain free if it is to prosper.

When we think of the history of our profession we realize that men of outstanding genius were always men of independent, unusual frame; and by their unique genius they made British medicine great. Surely it is only those who in their hearts regard greatness with envy who think that a State medical service is a good thing. I do not believe for one moment that such a service would appeal to first-class minds: with its pettifogging rules, its multitudinous forms, its endless negations, it could not do so. Instead, if this Service should come to pass, as it is envisaged by this Minister of Health, by this Government, it will come to be filled with a multitude of second-rate minds of a yes-man shape, who will make of British medicine an institution world-famous for its dull mediocrity, its small scientific exactness, the excellence of its statistics, and the envy the world over of the good bureaucrat. But this will not be the profession that could produce a Lister, a Harvey, a Moynihan, a Treves, and I do not believe that my great profession will meekly give up its freedom when the decisive day arrives.—I am, etc.,

Teignmouth, Devon. GEORGE A. F. QUINNELL.

SIR,—"And thus for nearly a year we have worked at the conference table to no purpose." And thus, too, do the Council add confirmation to the fears of many doctors that one of Mr. Bevan's type, creed, and expressed opinions has had from the beginning no intention of amending his Act and would prove impervious to conviction. Twelve months have

been spent in discussions with Ministry of Health officials, almost the net result of which has been to bring into sharper relief the difficulties and the pitfalls for the profession inherent in the Act. Indeed, one has the feeling that to describe such conversations as negotiations is altogether misleading and that the Committee's case could have been as well prepared in discussion among themselves with the help of legal advice, and also in half the time.

In the year that has passed all the business sides of a doctor's life as it concerns future plans have been completely held up. Behind a smoke-screen of secrecy the framework of the new Health Service has been steadily pushed forward, and doctor committee-men have taken their places among the planning authorities. Indeed, the words of the Council quoted above cannot be regarded as an overstatement, unless the delay has served the purpose of the Minister. We are now but little more than six months from the date of implementation of the Act, and still essentials and details are interlocked in a fog of uncertainty and confusion. For example, the sale and purchase of practice are defended in short and concise terms as an essential of continued freedom and efficiency, and then paragraph after paragraph is devoted to legalistic argument anent the difficulties that will arise if sale and purchase are abolished.

On which ground, then, are we prepared to join issue—on a principle of personal liberty or on the practical difficulty of working the Act as it stands? On this point it needs to be pointed out—and it cannot be too strongly emphasized—that the interests of the various sections of the profession are not identical. Of this a paramount example is again that of the sale and purchase of practice. This, though a sheet-anchor of independence and freedom as well as a guarantee of continuing efficiency to the general practitioner, is a matter of minor importance to the health officer or to the consultant. The hard truth should be faced without hypocrisy, for it is part of human nature, that men, or rather the great majority, will be more ready to disavow those principles in which they have no personal interest. Special weighting, therefore, should be allowed to the views of general practitioners in this matter.

In any event further equivocation and delay at this stage would be inexcusable and altogether intolerable. Argument and bargaining points must be put aside and the principles upon which we are prepared to stand fast decided. It is for the Council to strip themselves for action, and at the earliest possible moment to demand from the profession a plain yea or nay on simple issues which none can misunderstand.—I am, etc.,

Wirksworth, Derbyshire. E. D. BROSTER.

SIR,—The supporters of the National Health Service have decried the present medical services as being inefficient and out of date, and have drawn much attention to the inadequate accommodation and equipment of the surgeries and waiting-rooms in doctors' private houses. The public were told that under the new scheme they would have magnificent health centres, fully equipped with *x*-ray apparatus and laboratories and a team of doctors who would work regular hours and not be overworked. Now that we know the details the scheme is apparently merely to put the whole nation on the panel and thus accentuate the overcrowding of the already inadequate accommodation, and there is nothing new in it at all.

Mr. Bevan would have been wiser to have followed the example of General Montgomery, who made certain that every detail of his scheme was planned before taking action.—I am, etc.,

Camberley, Surrey. LESLIE HARTLEY.

SIR,—The doctors can accept the National Health Service Act or refuse it. The choice is theirs, they have but to exercise it. If they so will the Service cannot be forced upon them, for if 75% refuse to join on the appointed day then it cannot function, and an amending Act becomes a certainty—and that soon. The issue now before the profession is therefore remarkably simple and yet of transcendental importance, for it is nothing less than our freedom itself. On the one hand we may accept the Act as it now stands, entailing appropriation of our practices and remuneration by a basic salary—at first small to ensnare and delude us but at any time capable of increase by regulation to, mayhap, 99.9% at the will of the Minister without reference to Parliament—in short, complete loss of our freedom and liberty of action in a full-time State salaried service. Loss of our practices inevitably implies this loss of our freedom, a disaster to both doctor and patient alike.

On the other hand we may reject the present Act by refusing, in resounding majority, to join the Service and indicate this decision by a decisive negative in the forthcoming plebiscite. Such refusal, without doubt, will compel the introduction of an amending Act in which we will retain our practices and be remunerated by capitation fee alone. Thus may we assure our freedom without in any way sacrificing the interests of our patients, but on the contrary safeguarding them.

Either to accept thraldom on the appointed day or to seek service in the future under an amended Act that preserves both the liberty of the profession and the true interests of our patients is the crucial issue now before us. It must not be obscured by endless discussion of items of relatively little importance such as terms of service, remuneration, superannuation, etc. The fundamental consideration now is the future freedom of the profession or its serfdom—nothing less. That freedom is incompatible with service under the present Act. Finally, the profession itself holds the trump card, not the Minister. For pity's sake let us play it and answer in the plebiscite with an emphatic and overwhelming "NO."—I am, etc.,

Tiverton, Devon. R. E. J. PEMBREY.

The Minister's Gloss

SIR,—Your excellent leading article (Dec. 27, 1947, p. 1037) should be studied by all members of B.M.A. Beveridge's suggestion that it was not in the interest of the State to have sick people on disability funds caused the membership of B.M.A. to rise. The Coalition Minister of Health did listen to argument and was prepared to amend his White Paper when ousted from office. The present Act was heavily opposed by the Opposition in the House, as it is by most of one's patients, be they rich or poor. Sixty-four per cent of G.P.s rejected negotiation, but three great men of the profession overruled this, provided the Minister would consider fresh legislation.

The Minister has evaded this. Why another plebiscite? A year ago, faced with a panel strike, the Minister yielded to the weapon he knows so well. I forecast that this Act will have to be amended and that the stand of the profession will earn the gratitude of millions in this country.—I am, etc.,

Newquay, Cornwall. J. P. O'SHEA.

Congenital Pyloric Stenosis: Two Cases in One Family

SIR,—Mrs. X., aged 30, was delivered of a male infant. At six weeks the child was diagnosed as a congenital pyloric stenosis and operation performed. Feeding difficulties arose and gastro-enteritis followed, the infant dying 17 days later. Subsequently Mrs. X. was delivered of a boy and then a girl. When 39 she was delivered of an apparently normal male. Projectile vomiting appeared at the third week and one week later congenital pyloric stenosis was confirmed at operation. This infant is making good progress.—I am, etc.,

Wembley, Middlesex. M. B. STUNGO.

The Dangers of Going to Bed

SIR,—Our congratulations are due to Dr. R. A. J. Asher for his dissertation (Dec. 13, 1947, p. 967) on the dangers of going to bed or, more correctly, being confined to bed. I should like to add one more example of the untoward and contrary result arising from prolonged rest in bed. If we wish to stenose any part of the body immobilization is the accepted procedure. It is the common practice, as mentioned by Dr. Asher, to immobilize cases of rheumatic fever for a considerable period after the fever has departed. In bygone days months in bed was considered sound practice, with mitral stenosis as the inevitable end-result—the most serious of all valvular disorders.

Any barrier erected between the left auricle and the left ventricle must have a disastrous effect on the development of the left ventricle, which carries the burden of general circulation, and this is especially true in the growing heart. The present duration of rest after rheumatic heart disease is still too long, as evidenced by the incidence of obstructive mitral stenosis seen

in hospital practice. The incidence of rheumatic fever was found by Coombs to be 5 girls to 4 boys; yet the incidence of mitral stenosis in females must be in the region of 5 to 1 male. This is due to the less active life led by girls, who are seldom permitted to be out of range of the maternal eye; they sit and knit and acquire obstructive stenosis and provide most examples of auricular fibrillation in the forties. Her brother with the same diseases escapes to the playground and, despite restrictive advice, ensures that the cusps of the mitral valve are kept well apart by the vigour of his exercise, thereby securing a greater volume in flow and growth of the left ventricle. At the same time he prolongs his life.

Convalescent heart homes are not the nurseries for the cultivation of mitral stenosis that they used to be; nevertheless the introduction of the sedimentation rate has tended to increase bed rest in these cases, and mitral stenosis is actively encouraged once again. Because the sedimentation rate is increased, active endocarditis is presumed with often no justification; it might well be tonsil, sinus, or other infection. Immobilization and fibrosis are inseparable bed-mates and are no companions for growing hearts.—I am, etc.,

London, W.1. BRUCE WILLIAMSON.

Diet and the Nation's Health

SIR,—As a humble member of the profession I note with dismay that Dr. S. K. Westman (Dec. 6, 1947, p. 926) regards the Hunterian Society and frivolity as being synonymous. A press précis can be misleading; it is probable that he has now had access to the full discussion and is a wiser man. The comparative statistics given in his letter beg many questions, but this outstanding and alarming fact is borne out—namely, the famine babies of 1919–21 responded, in the absence of adequate food for the body, to a dangerous and devastating dietary of distorted mental and moral feeding. They contributed to the downfall of their country and plunged the civilized world into chaos and economic disaster. Was the subsequent prowess of Hitler Youth in war the triumph of starvation or the thrust behind a fanatical and insatiable ambition for power? In their quest for *Lebensraum* was it not perhaps a bigger dining-room they subconsciously sought?

While I admire Dr. Westman's personal victory of mind over matter, I would remind him that his unusual menu for strength is in short supply in this country. It would be regrettable if our rowing blues were deprived of their sport because they had nibbled their oars and sucked the substance of the boats while in training. The whittling down of our larder has already caused deterioration in our morale and bred dishonesty in many a decent home. The man in the street does not need a learned society to point that out to him. The desire for a high standard of food and health is not actuated by selfishness and greed on Britain's part, but in her upholding the terms of the Atlantic Charter—"that all the men in all the lands may live out their lives in freedom from fear and want." We want butter in our guns and so avoid any continental European or Asiatic parallels of hunger and discontent.—I am, etc.,

Dursley, Gloucestershire. ISABELLE B. S. FAYLE.

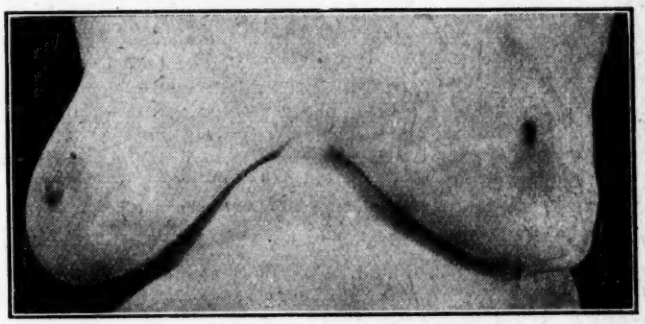
SIR,—May I add a note to Dr. F. M. R. Walshe's eloquent letter (Dec. 13, 1947, p. 971) emphasizing the importance of subjective impressions in the formulation of evidence? Sir Jack Drummond's argument seems to me to suffer from a fallacy of misplaced concreteness. He was mistaking the modern concept of nutrition for a fact, and forgetting that it is a theory still to be tested by experience. He maintained that, because we were getting all the items of diet which the modern theory of nutrition held to be necessary for our health, therefore we must be healthy. But this theory may prove to be inadequate, just as those theories of nutrition in vogue before the discovery of vitamins proved to be inadequate. It may be that from these subjective impressions which he scorns to notice new facts will emerge compelling the theory to be recast.

Of course, subjective impressions are dangerous data. The field they grow in may be thickly sown with the tares of wishful thinking. Disapproval of the Government's activities may easily squeeze itself through the gaps in our sentiment of scientific impartiality and emerge as subjective impressions concealing a grudge. This is what happened, no doubt, to those physicians who felt that their patients were suffering from the effects of calcium in the bread at a time when the calcium was present only in their imaginations. Much laborious and honest threshing is necessary to winnow away the chaff of adventitious percepts from the grain of a new impression. But it is the impressions which supply us with new facts and which therefore ought never to be neglected.—I am, etc.,

Wallingford, Berks. E. H. HARE.

A Sign of Carcinoma

SIR,—Carcinoma of the breast frequently presents one of the stiffest problems in surgical diagnosis, and all surgeons of experience approach these cases with humility, which is understandable when pathologists tell us that never a year passes by but they see at least one breast removed in the Halsted fashion for mastitis and more than one local removal of a carcinoma in error for a benign condition.



The simple manœuvre employed to obtain the accompanying photograph I have found after long experience to be a great help in diagnosis. If the arms are raised above the head as high as possible all the usual signs of carcinoma are increased and, if not already present, are frequently made manifest in the most surprising manner. This applies to the level of the nipples, retraction of the nipple, puckering of the skin, and even peau d'orange. In addition the palpability of the tumour to the flat hand is easier to elicit when the underlying muscles are on the stretch.

The case illustrated was referred to the out-patient department as a case of chronic mastitis, and with the arms hanging by the side the breasts were indistinguishable on inspection and the tumour was vague to the finger and impalpable to the palm of the hand. The raising of the arms above the head instantly made the diagnosis of malignancy indubitable. With chronic mastitis some puckering of the skin may be produced, but it is generally a diffuse rippling over a fair area rather than a well-defined depression such as is seen in the photograph. Feeling sure that others have made this discovery before, this simple test is nevertheless put forward in the hope that wider publicity for it will help in what must be regarded as one of the most responsible and difficult diagnoses which come the way of the clinician.—I am, etc.,

London, W.1. A. DICKSON WRIGHT.

Staphylococcal Infection due to Penicillin-resistant Strains

SIR,—In her very interesting article (Nov. 29, 1947, p. 863) Dr. Mary Barber draws attention to the increasing incidence of strains of *Staphylococcus pyogenes* that are grossly resistant to penicillin. We have been testing between April and December, 1947, all cultures of *Staph. pyogenes* for penicillin-sensitivity, using the penicillin-ditch method with 1, 5, and 10 units of penicillin per ml. Secondary cultures had been tested throughout. Out of a total of 115 cultures of *Staph. pyogenes*, 9 (7.8%) were penicillin-resistant.

Type of Infection.—Axillary abscess, 1; otitis media, 2; furunculosis, 1; dermatitis, 1; aplastic anaemia, 1 (blood culture). The 3 other penicillin-resistant strains were grown from the throat (2) and nose swabs (1) of carriers. Considering only the strains from infected cases, 6 (5.2%) were penicillin-resistant.

In Czechoslovakia, owing to the comparative shortage, the use of penicillin, especially in the form of ointments lozenges, etc., has not been as widespread as in Great Britain. None of the cases examined had received penicillin prior to the bacterio-

logical examination. Our figures might therefore indicate a "normal" rate of occurrence (about 5%) of penicillin-resistant strains of *Staph. pyogenes*.—I am, etc.,

Kosice, Czechoslovakia. I. FRIEDMANN.

Pica for Pipes

SIR,—I recently encountered rather an unusual instance of pica (craving for unnatural food) in pregnancy, which may be of interest to your readers. The patient, a woman of 36 years, had 14 pregnancies—10 full-term and 4 miscarriages. She was recently in hospital for her fourth miscarriage, with which she had a severe haemorrhage necessitating a blood transfusion. When she was later persuaded to swallow iron in the shape of ferrous sulphate for her still present anaemia, she declared she would sooner have some clay pipes to eat.

It transpired that during all her pregnancies (and most of her married life seems to have been spent in the pregnant state) she developed a craving for clay—generally in the form of clay pipes, which were, at one time at any rate, cheap to buy and easily procurable. She has good strong teeth and evidently experiences no difficulty in the mastication of the pipes, and when she cannot obtain the latter she eats pipe-clay, as used for cleaning stairs. She remarked jocularly that her doctor used to try and dissuade her from her practice by warning that she would give birth to "stooky weans." De Lee (1947) makes a reference to the desire for clay, among other unnatural foods, by certain pregnant women.—I am, etc.,

Bellshill, Lanarkshire. JOHN M. KING.

REFERENCE

De Lee, J. B., and Greenhill, J. P. (1947). *Principles and Practice of Obstetrics*, 9th edition, W. B. Saunders, Philadelphia, p. 83.

New South Wales Branch of B.M.A. and R.M.B.F.

SIR,—I hope you will allow me through your columns to record the indebtedness of the Royal Medical Benevolent Fund to the New South Wales Branch of the British Medical Association. All your readers will like to know of the great generosity of the members of the New South Wales Branch who have recently sent 360 food gift parcels to beneficiaries of this fund. This is such a warm-hearted and kindly action on the part of our colleagues overseas that I feel all members of the profession living in the home country will join with me in thanking our many friends in New South Wales.—I am, etc.,

ALFRED WEBB-JOHNSON,
President, Royal Medical Benevolent Fund.

POINTS FROM LETTERS

Splints from Spatulas

Mr. A. MACDIARMID (Thames, New Zealand) writes: Take an ordinary wooden tongue spatula and introduce it into the steam in a boiling sterilizer. To do this, lower the lid so that it holds the end of the spatula against the edge of the side of the sterilizer. Leave the spatula to steam for about a minute and then take it out. It is now pliable and can be bent to the desired shape between the fingers and thumb. It should be held thus until it dries, hardens, and maintains its shape. In this way it is easy to produce a curved splint or one with several angles of 45 degrees. The splint can be padded with a strip of adhesive felt. Do not put the splint in the water or it will become too wet.

Always in the House

A DOCTOR'S WIFE writes: "My dear, I never pass a day but I think how lucky you are to have a doctor in the house." . . . So speaks one of the best patients as one is laboriously toiling up the hill with a pram, having abandoned that wretched phone to the fates for an hour. Summer isn't quite so bad, but let me sympathize with all those other poor miserable creatures whose bed-companion is the telephone and whose days are spent keeping food eternally at a reasonable temperature so that the patient may have his doctor. Then, what of the evenings? Mentally and physically exhausted, the evening surgery done, and the last sickly patient tucked safely into bed, home comes the doctor to yet another sliding meal—eight, nine, ten—whatever the whim takes him. The newspaper, a pipe, and after a few minutes loud catarrhal snores. What a cheerful evening! Woe betide the wife who inquires for medical remedies at this juncture; they are doomed to be cast off as mere psychological flights of fancy. Better to keep one's thoughts of aching chilblains or children's spots deep in the crevices of the mind. What is there to it? One often wonders; and still every medical school pours out its numerous doctors, and a thousand crazy females go and land themselves into this heaven, with a doctor "always" in the house.

Obituary

G. F. STEBBING, M.B., F.R.C.S.

Mr. G. F. Stebbing, a pioneer of radiotherapy in this country and an outstanding personality, died at his home on Dec. 22 at the age of 63, after a long and painful illness, borne with characteristic optimism and courage. Like many other medical men he succumbed to a disease to the treatment of which he had devoted himself for many years.

George French Stebbing was educated at Guy's Hospital and qualified in 1906, taking the conjoint diploma and the M.B., B.S. with honours and distinction in surgery. After completing his house appointments he told Mr. Symonds, later Sir Chartres Symonds, whose house-surgeon he had been, about the kind of institutional work he would like to do. Sir Chartres replied that he knew of no such place and that Stebbing must create it for himself. In 1908 Stebbing went to the Lambeth Infirmary, and with the encouragement of the late medical superintendent, Dr. A. L. Baly, he developed the clinical side there and so rapidly raised the standard of work that by 1914 Lambeth Infirmary was held in high esteem by both the local populace and general practitioners. After a period of service in the Navy he returned to Lambeth Hospital, where he remained a leading light until the day of his death. In 1934 he was elected a Fellow of the Royal College of Surgeons and recently was a member of the Council of the College. He was made a Fellow of the Faculty of Radiology in 1939.

In his early years he devoted himself to all branches of medicine and surgery, and with his tremendous capacity for work and wide reading he became a "G.P." in the very best sense of the term. Many old Lambeth medical officers and nurses have reason to thank "Steb," or the "Great White Chief" as he was affectionately termed (he wore a long white coat not usual in those days), for all he taught them. His experience was so great that his phrase, "I am quite familiar with that," disappointed many a junior colleague who felt he had produced a problem for his chief.

Some twenty-five years ago Stebbing became interested in the use of radium for the treatment of malignant disease, and in 1929 arrangements were made between the Lambeth Board of Guardians and the Ministry of Health to provide Lambeth Hospital with radium and deep *x*-ray therapy plant, which was to be available for the treatment of patients not only from the district but from any part of London. Stebbing visited all the principal clinics in this country and on the Continent, and the information he obtained was applied in equipping the new department. As a first-class surgeon and radiotherapist, a rare combination, he achieved great success in a great number of patients, and even when this was not possible the confidence that he inspired and the infinite pains he took with palliative measures brought comfort to many sad cases.

Stebbing will always be remembered by his contemporaries for his wide interests both inside and outside the hospital. He was a member and honorary secretary of the Radium Commission from its formation in 1929. He was chairman of the London and Counties Medical Protection Society. He was largely responsible for the establishment of the L.C.C. Clinical Research Committee and was its first chairman. From this there developed the L.C.C. Medical Society, of whose first council he was chairman. He was also for many years examiner in radiology for the Conjoint Board. He had the faculty of always being able to interest himself in anything which interested his friends and acquaintances. He was a fine team worker and was never found unwilling to see any case a colleague desired him to see. An American visitor to his clinic once described him as the "human dynamo," a tribute to his amazing energy. His direct approach to the things that mattered and his dislike of non-essentials were characteristic. He inspired complete confidence and affection in his patients and he could remember them years afterwards and what he had done for them. He was a fine lecturer and clinical teacher.

The L.C.C. Public Health Department, and particularly Lambeth, will miss him sadly, and the sympathy of the whole staff goes out to his wife, his married daughter, and the two sons, both doing medicine, who survive him.—A. D.

Sir E. Rock Carling writes: Mr. Stebbing's activities were numerous and widespread. To them all he brought the same inexhaustible energy and enthusiasm. Whatever he did he did with his might, whether as medical secretary of the Radium Commission, as chairman of Council of the Medical Protection Society, as a member of the Cancer Committee and other committees of the Ministry of Health, of the Faculty of Radiologists, or the Medical Research Council's Nuclear Physics Committee, or a dozen other bodies upon which he served. All that, too, was work of supererogation, for he filled the double post of surgeon in charge of a division at the Lambeth Hospital and radiotherapist-in-chief. Stebbing held his views with tenacity. He formed them upon what he believed to be fundamental premises and permitted no deviation. He was utterly free from self-interest, and, if not entirely devoid of ambition, his aims and object had no taint of personal advantage. He wished to exert his influence to the full in the interests of sound and safe treatment for the sick. To that extent he sought positions whence he could apply his influence, but certainly without thought of reward other than a just prestige. He was no respecter of persons but generous in his appreciation of the worth of other men whose work he could admire. His habitual cheerfulness, his sense of the comic, his genuine friendliness made him loved by those who knew him well. His transparent integrity, his professional skill and competence, his upright character, all combined to secure him the esteem and admiration of his colleagues.

Mr. Malcolm Donaldson writes: The death of George Stebbing is not only a very great sorrow to his many friends but a serious loss to the forces ranged against cancer. He was a man of outstanding character and quite fearless in expressing his views. One of the foremost radiotherapists of his time, his work in connexion with the formation of the Faculty of Radiologists is well known, but perhaps his greatest work was done with the National Radium Commission. It is no exaggeration to say that the success of the Commission was largely due to his personality and unbounded energy. Being a general surgeon as well as a radiotherapist he realized that the treatment of cancer cannot be kept in watertight compartments but must be considered as a whole. It was in connexion with the Commission that I first met Stebbing, and the more I saw of him the more I liked and admired him. He was one of the "whitest men" with whom it has been my privilege to serve.

SIR BERNARD SPILSBURY, M.B., F.R.C.P.

Dr. G. Roche Lynch writes: I would like to pay a tribute to the memory of Spilsbury and his medical work, for no one in this country during the last forty years has done more for this subject, which in turn has led to the production of adequate and accurate scientific work for evidence in the criminal courts. Many times have judges complimented him upon his clear, lucid, and accurate evidence. His energy, thoroughness, and capacity for detail are by-words, but I would like to add that the investigation only commenced in the post-mortem room, to be followed up by careful laboratory work, in turn to be followed by many hours of quiet assessment of all the material facts in his study. Thus his final opinion was made after a judicial weighing up of the facts, and it would be doing him a great wrong if it were suggested that he was a witness for the prosecution.

All his life he overworked, and in the later years he continued to do so well knowing that his heart was not strong and that prudence dictated a less energetic mode of life. It is a matter of great regret that he has not left any record of his cases, for this would be of inestimable value to future workers in this field. But his excuse would have been a genuine one—namely, he had no time. Perhaps one of the most important results of his work—one which cannot be overstressed—is his influence upon coroners. When Spilsbury commenced to work for them they employed but few trained pathologists and the work was not of a very high order. Nowadays, thanks to him, coroners have realized the importance of the employment of trained pathologists.

Spilsbury was a very human person and a delightful companion. When away in the country on a long case at the assizes one could not wish for better company and he had a gift of making friends. He was very conscious of the difficulties of the doctor who was suddenly confronted with a serious criminal case and would do everything in his power to make things easy for him.

A correspondent writes: Bernard Spilsbury's professional eminence and skill are too well known to need any eulogy—this is intended rather as a personal tribute to a great man by one who has been privileged to enjoy his friendship for more than twenty-five years. It began by our common membership of a society in which we were both interested and in which not long afterwards we had the honour of holding joint office for several years, Spilsbury later becoming one of its most distinguished presidents. He was one of the most truly modest and humble-minded men I have ever known, for although I am convinced that he knew quite well that in that branch of medicine which he had made his own he stood pre-eminent and without a rival, yet he never spoke of himself or his own achievement, and both hated and, so far as he possibly could, shunned the public notice which was inevitably thrust upon him. His complete absorption in his work was for the sake of the work itself and the advancement of the ends of justice and true knowledge, not for any personal distinction.

Spilsbury was a devoted son of Oxford and of his own College, Magdalen, where he was an honorary member of Common Room, and he used to delight in recalling his own undergraduate days. He preserved in later life much of the gaiety and almost boyish high spirits which usually belonged to much younger men, and I used often to marvel how he was able to do so under the burden of his always exacting, and often grim, professional work. His later years were greatly burdened by the loss of his two elder sons, the younger of whom had just qualified and obtained a house appointment at St. Thomas's when he was killed while on duty in one of the early air raids in the autumn of 1940. The elder son, whose health had never been robust, died in 1945. Notwithstanding these blows he still kept at his work, his capacity for which was enormous, and there was no five-day week or eight-hour day for him. What was to me one of Spilsbury's most striking characteristics as a medical witness was his great sense of fairness, and I believe that this was the general impression of the public who followed with so much interest the notable trials in which he was concerned. His evidence was always directed not to the securing of a conviction, but to the ascertainment of the truth and to the fulfilment of justice, and whenever anything was to be said in favour of an accused person one could be quite sure that Spilsbury would say it. The professions of both medicine and law will deplore his passing, and those who, like myself, have known him as a friend will be the poorer for the loss of one whom to have known as such was in itself both an education and a source of pride.

Dr. HAMISH FALCONER MASSON died suddenly, from coronary thrombosis, on Dec. 7, at the early age of 45. The third son of the late George Masson, J.P., of Kingussie, he was educated at Fettes College and Edinburgh University, where he took the M.A. in 1923. In 1926 he graduated M.B., Ch.B., and passed the examination for the F.R.C.S.Ed. in 1930. After house appointments at Preston Royal Infirmary and Kettering he was for a time in practice in Dingwall before settling in South Woodford, where he had practised for the last ten years. Hamish Masson had intellectual gifts and a personality that could have carried him to a high place among consultants, but he preferred general practice with its more personal human contacts. As a general practitioner he was immensely popular and built up a large practice in South Woodford. His handsome appearance made him a conspicuous figure in any company, but no man so gifted was ever more unassuming or more tolerant towards his fellow men. His work made great demands upon him, and he never spared himself. In the last year his health gave some grounds for anxiety, but the end, when it came, was quite unexpected. On Dec. 13 a memorial service was held at All Saints' Church, Woodford Green, Essex. A crowded church was evidence of the respect and affection in which Dr. Masson was held. He will be gratefully remembered in Woodford as a good doctor.—J. B. Y.

Medical Notes in Parliament

The Medical Practitioners and Pharmacists Act received the Royal Assent on Dec. 18.

The Children Bill to make further provision for the care and welfare of boys and girls when without parents, or living away from their parents, or when their parents are unfit or unable to take care of them, and to end the Young Persons Act, 1933, and other Acts, was read a first time in the House of Lords on Dec. 18.

First readings were given in the House of Commons on Dec. 18 to the Attempted Rape Bill, and to the Animals' Bill, extending the period during which payments can be made for eradication of bovine tuberculosis.

The Report of the Committee of the Privy Council for Medical Research and the Report of the Medical Research Council for the war years 1939–45 were presented to Parliament on Dec. 18.

Venereal Disease.—On Dec. 11 Mr. SORENSEN asked against how many men and women had complaints been lodged in respect of suspected V.D. in the Metropolitan Police area during the past twelve months. Mr. BEVAN replied that figures were not kept for the Metropolitan Police district, but in London and the Home Counties reports were received about 54 men and 875 women in 1946, compared with 37 men and 2,679 women in 1945. The number who received treatment was not available. He added that the figures showed the position was not unsatisfactory.

Health Education.—Mr. HASTINGS, on Dec. 18, asked the Minister of Health whether in view of the important part that prevention must play in the new National Health Service, and the consequent need for guidance of officers of local authorities in health education matters, he would increase the support, financial and otherwise, given by his Ministry to the Central Council for Health Education. Mr. BEVAN answered that the nature and financing of the services to be provided by the Central Council after the appointed day were still under discussion between his officers and representatives of the Council and of local authorities.

Obstetric Analgesia.—The number of cases where analgesia was provided by domiciliary midwives increased from 7,262 in 1945 to 20,507 in 1946. The number of midwives trained to give it had doubled in the current year.

Milk.—The average weekly consumption of milk under the Milk in Schools Scheme during October, 1947, is estimated to have been 980,000 gallons, which represents a weekly average of approximately 1.6 pints (908 ml.) per child taking milk.

Mass Radiography.—There are 22 mass radiography outfits working in England and Wales. For the first six months of this year the number of persons examined averaged about 50,000 a month.

Penicillin.—Current production of penicillin in the United Kingdom averages 520,000 mega units a month and is increasing. It involves no charge on public funds.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

Geoffrey Wingfield Harris, M.D., has been appointed Lecturer in Physiology, with tenure to Dec. 31, 1949, and seniority from Jan. 1, 1947.

The following degrees were conferred on Dec. 13, 1947:

M.D.—J. H. Walters, T. C, N. Gibbens, V. H. Wilson.

The following candidates have been approved at the examination indicated:

FINAL M.B.—*Part II (Principles and Practice of Physic, Pathology and Pharmacology).* M. S. Adams, P. S. Andrews, J. H. Angel, C. P. Atkin, J. R. Bennett, J. G. Bennette, H. C. H. Bird, M. D. M. Bowen, P. H. Bright, M. H. Clement, D. Cooper, J. D. Cox, J. H. Cule, J. M. Frew, R. G. Gibbs, M. T. Gillies, E. H. Griffiths, N. H. Harris, O. E. F. Hodgson, C. B. Holmes, M. C. Hudson Bennett, D. A. P. Hunt, W. N. Ingham, J. H. Inskip, J. S. Jenkins, A. H. Jones, H. W. H. Kennard, R. V. Knight, F. R. Lambert, M. G. H. Lewis, W. Lewis, A. A. McInnes, J. E. MacIver, I. K. R. McMillan, R. K. Mason, F. S. Mellows, D. J. Morton, D. S. Paine, J. C. R. Payne, A. I. D. Prentice, J. Prestt, L. C. Robson, R. C. Roxburgh, M. H. Russell, J. D. Scott, B. E. Shairp, P. H. A. Sneath, K. C. G. Taylor, J. P. D. Thomas, M. B. Thompson, F. G. Tomlins, J. D. G. Turner, D. H. H. Walford, G. G. Walker, B. M. Watney, J. O. M. Wedderburn, J. D. Whitby, D. Whitfield, H. B. L. Williams, K. L. Williams, H. L. J. Wilson, G. E. W. Wolstenholme, G. M. Woodwark. *Women:* B. Jones, A. E. Perkins.

UNIVERSITY OF EDINBURGH

At a graduation ceremonial on Dec. 19, 1947, the following degrees were conferred:

M.D.—T. M. Abbas, [2]A. W. Branwood, F. S. Fiddes, S. L. Forrest, [1]J. A. L. Gilbert, [2]J. W. Rae, S. A. Rahman (*in absentia*).

PH.D.—In the Faculty of Medicine: M. L. Bayoumi, M.B., Ch.B.

M.B., Ch.B.—A. McD. Allan, H. W. Bisset, G. Brown, Margaret W. Brown, Jean Buchanan, F. G. Cumming, I. H. P. Doherty, T. H. Donaldson, L. A. Gess, R. R. Gillies, A. Girby, G. T. Graham, Janet Hazell, L. J. M. Jamieson, H. A. Jones, H. M. Kirkpatrick, F. E. Kohler, R. G. Krause, Marjorie V. Kydd, Anne M. McCartney, B. T. Mulligan, A. M. Nelson, W. H. Nisbet, Susan B. G. Ofori-Atta, J. G. Parish, A. G. B. Poole, A. D. Ross, Jean R. W. Ross, K. Saltman, D. A. Smith, B. J. Sproule, Diana Stewart, Leila M. Wojtczak (*née* Sinha), Lesley L. D. Wood.

[1] Highly commended for thesis.
[2] Commended for thesis.

UNIVERSITY OF DURHAM

In a congregation on Dec. 19, 1947, the following medical degrees and diploma were conferred:

M.B., B.S.—Anna Book, H. M. Brand, H. C. Brown, J. D. Brown, J. H. Grant, Brenda M. Hilton, A. R. Horler, A. A. Lawson, K. M. Martischnig, W. H. Raine, A. Rounding, J. R. W. Sinton, R. Whitfield, P. E. I. Winburn, K. M. Wood.

B.D.S.—C. H. Tonge, M.B., B.S.

UNIVERSITY OF LEEDS

At a meeting of the council held on Dec. 17, 1947, George Norman Myers, M.D., F.R.C.P., was appointed to the newly instituted post of Director of Research in Rheumatism.

UNIVERSITY OF SHEFFIELD

At a meeting of the University Council on Dec. 19, 1947, Ronan O'Rahilly, M.Sc., M.B., B.Ch., was appointed Lecturer in Anatomy and John Lewis Emery, M.D., D.C.H., Honorary Lecturer in Pathology.

The Council received the resignation by Dr. T. Jones of the post of Demonstrator in Anatomy and thanked him for his services to the University.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a meeting of the Royal College of Surgeons of Edinburgh held on Dec. 17, 1947, with Mr. Frank E. Jardine, President, in the chair, the following candidates, having passed the requisite examinations, were admitted Fellows: M. G. Allen-Mersh, N. Ameli, G. S. Anderson, Una Aranha, A. J. S. Burger, B. Z. Claman, T. R. B. Courtney, R. D. Cowan, T. T. Davies, A. L. Deacon, J. L. Douglas, W. Drummond, G. E. Dunkerley, J. R. Elder, C. D. Falconer, W. D. Giffen, J. S. Glennie, J. T. Gray, L. M. Greene, G. I. Henderson, N. G. C. Hendry, S. Henson, F. G. Hibbert, W. P. Hirsch, J. R. Hughes, T. B. Hutton, H. B. Jackson, I. Jacobson, J. Jankowitz, J. H. Jordan, P. F. King, R. G. R. Langford, M. D. Leitch, G. S. Lester, A. M. Loughran, A. Lurie, W. A. McAlpine, J. N. W. McCagie, V. V. McCusker, A. McDougall, J. A. Macfarlane, J. G. McFetridge, K. MacI. MacKenzie, G. C. McKinlay, L. A. H. McShine, W. A. W. Maney, M. J. Maxwell, L. Mirkin, W. Murdie, D. S. Murray, J. F. Neil, M. W. Paterson, R. H. Purnell, B. Ramamurthi, J. I. Rossman, J. E. Rowlands, M. P. Shapiro, E. G. F. Shaw, R. H. Simpson, S. R. Sinclair, M. S. Sindhu, T. S. Stewart, C. R. Strother-Stewart, S. D. Stock, I. S. D. Thomson, J. D. Thomson, A. K. Toufeeq, W. A. L. Tucker, H. P. Watson, A. L. Webster, T. B. Whiston, G. W. Wigg, H. W. G. Williams, H. O. Williams, J. E. Wilson, H. C. Worrall, Margaret P. Yeoman, G. B. Young, I. S. Young, H. Zalin.

SOCIETY OF APOTHECARIES OF LONDON

Meetings of the Court of Assistants of the Society were held on Oct. 28 and Dec. 16, 1947, with the Master, Prof. E. C. Dodds, F.R.S., in the chair. Past Masters' Medals were conferred upon Dr. J. Prescott Hedley and Dr. Hugh Powell. The reports of the deaths of Dr. Russell E. Palmer, a retired Member of the Court, and Group Captain Henry Cooper, late Clerk and Registrar of the Society, were received with great regret. The following were appointed representatives of the Society: on the General Medical Council, Dr. Hedley; on the Committee of Honour of the Fourth International Congress of Otolaryngology, Prof. Dodds; on the Central Council for District Nursing in London, Mr. George Wynn-Williams. Dr. Archibald Gilpin was appointed Archivist to the Society in succession to the late Dr. Cecil Wall.

The diploma of M.M.S.A. was granted, upon examination, to A. M. Michaelowsky.

The diploma of L.M.S.S.A. was granted, upon examination, to the following successful candidates: J. N. Phillips, H. R. Mohammed, F. A. R. Bateman, H. Burns-Price, A. A. Collis, M. E. Cowan, J. M. Cowan, G. R. Davies, R. Worsley, R. J. Helyer, D. M. H. Bickmore, D. G. Buchanan, J. C. Bradley, P. Benham, D. G. Walworth-Furness, J. M. Scott, K. Y. Khong, D. M. Strange, E. Wales, C. J. Burrows, H. S. Baar.

No. 50

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended Dec. 13.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each Infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1947					1946 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	64	6	18	1	—	31	3	25	—	1
Deaths		2	—				2	—		
Diphtheria	233	19	67	14	10	328	16	87	33	14
Deaths	4	—	—	2	—	3	—	3	3	—
Dysentery	106	7	28	1	—	68	13	16	4	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	1	—	—	—	—	—	—	—	—	—
Deaths		—					—			
Erysipelas			29	14	2			51	9	3
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				22					36	
Deaths	62	7	19	3	2	63	7	14	17	1
Measles*	3,379	156	410	192	20	6,957	243	318	50	219
Deaths	1	—	—	—	—	6	—	3	1	1
Ophthalmia neonatorum	58	4	8	1	—	43	3	10	—	—
Deaths										
Paratyphoid fever	3	1	—	—	—	5	1	1 (B)	2 (B)	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal	723	29	8	3	5	693	62	12	6	6
Deaths (from influenza)†	23	2	5	2	—	22	2	2	—	—
Pneumonia, primary			319	22				335	29	
Deaths		53		11	14		35			7
Polio-encephalitis, acute	7	3				—	—			
Deaths		—					—			
Poliomyelitis, acute	77	4	11	4	5	14	—	2	5	1
Deaths		—					—			
Puerperal fever		2	10		—		3	7		—
Deaths										
Puerperal pyrexia‡	116	9	9	4	—	148	8	16	1	—
Deaths		1					—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,939	131	296	32	44	1,392	101	332	35	41
Deaths	2	—	—	—	—	—	—	—	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	10	—	4	4	—	7	1	—	5	1
Deaths	—	—	1	—	—	1	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	1,737	92	38	29	5	1,664	96	273	57	40
Deaths	4	—	—	—	—	7	1	1	—	—
Deaths (0–1 year)	389	41	79	19	25	495	61	69	53	13
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	5,493	817	804	200	159	5,297	887	649	249	127
Annual death rate (per 1,000 persons living)			16·7	12·6				14·3		
Live births	8,044	1367	945	419	252	9,440	1464	1102	416	279
Annual rate per 1,000 persons living			19·0	26·4				22·2		
Stillbirths	236	36	26			296	42	39		
Rate per 1,000 total births (including stillborn)			27					34		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

‡ Includes puerperal fever for England and Wales and Eire.

EPIDEMIOLOGICAL NOTES

Poliomyelitis

For the first time since the peak figure of the week ended Sept. 6, notifications of poliomyelitis in England and Wales for the week ended Dec. 13, 77 (70), and of polio-encephalitis 7 (6), were slightly higher than in the preceding week. Figures for the week ended Dec. 6 are given in parentheses. The only county showing a definite rise was Somerset 5 (0), otherwise the increases were in ones and twos and were scattered throughout the country. A further fall was shown, however, in the figures for the week ended Dec. 20, when there were notified 55 cases of poliomyelitis and 5 cases of polio-encephalitis.

Discussion of Table

In *England and Wales* infectious diseases were more prevalent during the week. A rise in the number of notifications was recorded for every disease except scarlet fever, which declined by 88. There were increases in the incidence of measles 580, whooping-cough 249, acute pneumonia 193, diphtheria 28, cerebrospinal fever 18, dysentery 13, and typhoid 10.

The largest increases in the local incidence of measles were Yorkshire West Riding 88, Cornwall 46, Glamorgan 74, and Staffordshire 70; the only large decrease was Surrey 86. The incidence of whooping-cough increased in each region except in the south-western counties and Wales; the most notable rise was Lancashire 62.

The largest increases in the notifications of pneumonia were those of Yorkshire West Riding 42 and Lancashire 30. The only significant variation in the local trends of diphtheria was a rise of 14 in Essex. No changes of any size occurred in the local trends of scarlet fever.

Of the 10 cases of typhoid fever 6 were notified in Lancashire, Warrington R.D. An outbreak of dysentery involving 9 persons was reported from Sussex, Petworth R.D. A rise in the notifications of dysentery occurred in Yorkshire West Riding, from 3 to 27; the cases were scattered throughout the county.

The notifications of acute poliomyelitis after declining for thirteen consecutive weeks showed a rise of 7. The chief feature of the returns for poliomyelitis was a rise from 17 to 32 in the combined areas of London and the south-eastern and south-western counties.

In *Scotland* increases were recorded in the notifications of measles 39 and diphtheria 29, and decreases were reported for scarlet fever 41, acute primary pneumonia 21, and whooping-cough 15. A small increase in the incidence of diphtheria was recorded in most regions; the largest local rise was in Glasgow, where the cases rose from 16 to 30.

In *Eire* there were decreases in the incidence of scarlet fever 23, whooping-cough 19, diphtheria 14, and measles 12. In contrast to the general trend increases in the notifications of measles were recorded from Wicklow, Bray U.D. 15, Wexford, Enniscarthy 16, and Dublin C.B. 16.

In *Northern Ireland* the notifications of measles increased by 19 and those of scarlet fever fell by 15. The rise in the notifications of measles was mainly due to an outbreak in the urban district of Portrush with 15 cases.

Medical News

I.S.T.D.

A course of six lectures on "Delinquency and the Educator" will be given by Miss Barbara Low at the Institute for the Scientific Treatment of Delinquency, 8, Bourdon Street, London, W., on Jan. 27 and Feb. 3, 13, and 24, and March 2 and 9, 1948, at 6.30 p.m. The fee for the course is 15s. (single lecture, 3s.).

Ulster Medical Society

After a lapse of nine years the Ulster Medical Society held its Annual Dinner on Dec. 11, Mr. G. R. B. Purce, the president, being in the chair. The attendance of Fellows and guests was limited by Ministry of Food regulations, and many who would have welcomed the opportunity of resuming this happy annual occasion were unable to be present. The Honorary Fellowship of the Society was conferred upon Prof. F. J. Browne, Mr. James A. Craig, Mr. S. T. Irwin, Prof. C. G. Lowry, Mr. Howard Stevenson, M.P., and Sir Henry Tidy.

Tubercle

The Tuberculosis Association has adopted *Tubercle* as its official organ; the January issue of the journal carries notice of the change on its cover and includes Dr. Frederick Heaf's Presidential Address to the Association.

H.S.A. Scholarships for Nurses

The Hospital Saving Association will award scholarships in 1948 for trained nurses as follows, the approximate values being shown: Nursing administrators, £196 each; nursing administrators (public health), £196 each; nurse dietitians, £340 each; sister tutors, £203 each; tutors to health visitors, £203 each; health visitors, £126 each; industrial nurses, £143 each; midwife teachers, £78 each. The H.S.A. will later determine the number of each kind of scholarship to be awarded and reserves the right to withhold any scholarship if there are too few suitable candidates. The scholarships will be available for the courses at any of the recognized training centres. They are open to nurses who (*a*) are registered on the general part of the State Register and (*b*) have graduated in a voluntary or local-authority hospital within the area of King Edward's Hospital Fund for London. Applications must be made before Jan. 31, 1948. Particulars may be obtained from: The Director in the Education Department, Royal College of Nursing, 1a, Henrietta Place, Cavendish Square, London, W.1.

Donations to Institute of Child Health

The province of Natal has recently given £106,888 to the Institute of Child Health of the University of London, and an anonymous donor has given £5,000 to establish a lectureship in memory of the late Mr. A. Simpson-Smith, formerly surgeon to the Hospital for Sick Children, Great Ormond Street. The Institute was established in 1946 and is accommodated at the Hospital for Sick Children. The demand for postgraduate teaching considerably exceeds the facilities available, but it has been met in part by clinical out-patient teaching at the Queen Elizabeth Hospital for Children, Hackney Road. Teaching on the new-born baby is given at the British Postgraduate Medical School, Hammersmith. The Institute also conducts research at the Great Ormond Street Hospital, and recently a genetics department has been established to study hereditary disorders. It is proposed to have a new building for the Institute as near as possible to the Great Ormond Street Hospital. These munificent gifts are especially timely, for plans are being made to expand the Institute.

COMING EVENTS

Socialist Medical Association

An inaugural meeting of the North-west Middlesex Branch of the Socialist Medical Association will be held at Wembley Town Hall on Jan. 8 at 7.30. Dr. Eileen Warren will speak on "The Socialist Medical Association and the New National Health Service."

St. George's Hospital Medical School

A series of neurological and psychiatric lecture-demonstrations, which began at St. George's Hospital Medical School, Hyde Park Corner, London, S.W., on Jan. 1, will be continued weekly on Thursdays, at 4.30 p.m., until March 18. The lecture-demonstrations are open to all medical practitioners and senior students, without fee.

National Congress on Cancer

The third National Congress on Cancer will be held in Havana from Feb. 23–28, 1948. Further information may be obtained from the Organizing Committee of the Anti-Cancer League, whose offices are at F.Y. 29, Vedado, Havana. Among other contributions papers will be read at the Congress on cancer of the lung, bladder, and uterus.

SOCIETIES AND LECTURES

Sunday

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Woburn House, Tavistock Square, London, W.C., Jan. 4, 3 p.m. "*Some Chemical and Biological Properties of Antibiotics.*" E. Chain, M.A., Ph.D.

Tuesday

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, W.C.—Jan. 6, 5 p.m. *Pathological Demonstrations.* Dr. I. Muende.

Thursday

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—Jan. 8, 4.30 p.m. *Neurological Lecture-demonstration.* Dr. A. Feiling.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, W.C.—Jan. 8, 5 p.m. "*Cutaneous Tuberculosis.*" Dr. G. B. Dowling.

Friday

LONDON CHEST HOSPITAL, Victoria Park, E.—Jan. 9, 5 p.m. "*Spontaneous Pneumothorax.*" Dr. J. Smart.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—Jan. 9, 8 p.m. "*Some Physical Signs in Clinical Surgery.*" Address by Mr. Hamilton Bailey.

APPOINTMENTS

LONDON COUNTY COUNCIL.—The following appointments have been made at the hospitals indicated in parentheses: *Senior Physicians* (*Superintendents*): J. C. Evans, M.R.C.S., M.R.C.P. (St. Charles'); W. Feldman, M.D., M.R.C.P. (St. Giles); W. G. Sears, M.D., M.R.C.P. (Mile End); B. A. Young, M.D., M.R.C.P. (St. Alfege's). *Physician Superintendents:* J. S. Anderson, M.D. (Grove); J. V. Armstrong, M.D. (Brook); H. S. Banks, M.D., F.R.C.P. (Park); N. D. Begg, M.D. (North-Eastern); F. J. Bentley, M.D., F.R.C.P. (High Wood Hospital for Children); J. C. Blake, M.B., B.S. (South-Western); W. C. Fowler, M.D. (Pinewood Sanatorium); W. Gunn, M.B., Ch.B., F.R.C.P. (North-Western); W. H. Kelleher, M.D. (Western); M. H. Logg, M.D. (Grove Park); G. W. Ronaldson, M.D. (Eastern); W. E. Snell, M.D., F.R.C.P. (Colindale); J. Watt, M.D. (King George V Sanatorium). *Surgeon Specialists* (*Superintendents*): W. P. Greenwood, M.D., F.R.C.S. (Bethnal Green); R. A. V. Lewys-Lloyd, F.R.C.S. (St. Olaves); J. McN. Milloy, F.R.C.S. (St. Mary Abbots); J. E. Piercy, F.R.C.S.Ed. (New End); J. R. M. Whigham, F.R.C.S. (St. Andrew's). *Senior Physicians* (*Deputy to Superintendents*): H. C. Aston, M.B., Ch.B., M.R.C.P. (Bethnal Green); R. D. Green, M.D., M.R.C.P. (Paddington); T. St. M. Norris, M.B., B.Chir., M.R.C.P. (Archway Group of Hospitals, Highgate); D. W. G. Smith, M.B., Ch.B., M.R.C.P. (St. Andrew's); M. Toohey, M.D., M.R.C.P. (New End); C. E. W. Wheaton, M.D., M.R.C.P. (Lambeth). *Assistant Senior Physicians* (*Deputy to Physician Superintendents*): G. E. Breen, M.D. (Brook); J. W. Healy, M.D. (Eastern); L. J. M. Laurent, M.D., M.R.C.P. (Park); W. J. P. Lillis, L.R.C.P.I. and L.M. (Western); J. J. McCann, M.B., B.S., M.R.C.P. (Pinewood Sanatorium); J. C. J. McEntee, M.D., M.R.C.P. (Grove); D. Porter, B.M., Ch.B. (King George V Sanatorium); A. M. Ramsay, M.D. (North-Western); W. F. Richards, M.B., B.Ch., M.R.C.P. (High Wood); R. Swyer, M.R.C.S., L.R.C.P. (North-Eastern). *Surgeon Specialists* (*Deputy to Superintendents*): H. L. Cochrane, F.R.C.S. (Fulham); G. S. Ferraby, M.S., F.R.C.S. (St. Charles'); J. Gabe, F.R.C.S. (St. Alfege's); J. C. Gillies, F.R.C.S.Ed. (Hackney); S. W. Holmes, F.R.C.S. (Mile End); I. W. Matheson, F.R.C.S. (St. Giles); I. I. Price, F.R.C.S. (Archway Group of Hospitals, Highgate); K. F. D. Waters, F.R.C.S.Ed. (St. Stephen's). *Senior Physicians:* J. A. Cardno, M.D. (Hackney); B. Freedman, M.B., B.S., M.R.C.P. (Dulwich); B. Gottlieb, M.D., M.R.C.P. (St. Mary Abbots); P. Harvey, M.D., M.R.C.P. (St. Stephen's); A. Kahan, M.D. (St. James); J. H. G. Mason, M.D., M.R.C.P. (St. Olaves); H. E. S. Pearson, M.D., M.R.C.P. (Archway Group of Hospitals, Highgate). *Surgeon Specialists:* T. J. Eason, F.R.C.S. (Lambeth); A. N. McCrea, F.R.C.S. (Dulwich); H. K. Vernon, M.S., F.R.C.S. (St. James); R. H. Metcalfe, M.Chir., F.R.C.S. (St. James, and Queen Mary's Hospital for Children, Carshalton); R. C. F. Catterall, M.Chir., F.R.C.S. (St. Alfege's, and Queen Mary's, Sidcup). *Assistant Surgeon Specialist:* R. Glyn Thomas, F.R.C.S. (Queen Mary's Hospital for Children, Carshalton, and St. James (deputy at the former)).

JONES, T. B., M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, Royal Eastern Counties Institution, Ltd., Abbeygate House, Colchester.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Bintcliffe.—On Dec. 19, 1947, to the wife of Lieutenant-Colonel E. W. Bintcliffe, M.B.E., M.S., F.R.C.S., a son.

Holloway.—On Dec. 19, 1947, at Selly Oak Hospital, Birmingham, to Dulcie (*née* Callis), wife of Dr. H. J. Holloway, a daughter—Ann Michele.

Laurie.—On Dec. 17, 1947, at Gwyn Mor Nursing Home, Cardiff, to Sybil, wife of Lieutenant-Colonel W. Laurie, D.S.O., I.M.S., a son.

Peberdy.—On Dec. 25, 1947, at 5, Tankerville Place, Newcastle-upon-Tyne, 2, to Mary (*née* Laws), wife of Dr. Geoffrey Peberdy, a sister for Karen—Noel Marion.

DEATHS

Beatty.—On Dec. 24, 1947, Robert Moorhead Beatty, M.B., B.Ch., of Westfield House, Heckmondwike, Yorks, aged 82.

Broughton-Alcock.—On Dec. 23, 1947, at Chiswick, William Broughton-Alcock, M.B.

Collins.—On Dec. 23, 1947, Henry Nathan Warner Collins, M.D., D.M.R.E., of 50, Putney Hill, London, S.W.

Davies.—On Dec. 16, 1947, at 176, Hamstead Road, Handsworth, Birmingham, Arthur James Davies, M.B., Ch.B., M.R.C.P., aged 50.

Goitein.—On Dec. 17, 1947, at 7a, Basing Hill, London, N.W., Bernard Goitein, L.S.A., aged 76.

Ingram.—On Dec. 20, 1947, at 42, Westby Road, Bournemouth, Arthur Charles Ingram, M.D.

Jobson.—On Dec. 19, 1947, at St. Thomas's Hospital, London, S.E., Eric William Charles Jobson, M.B., Ch.B., Colonial Medical Service.

Johns.—On Dec. 23, 1947, at Netherleigh, Lansdown Road, Cheltenham, John Francis Johns, M.D.

Johnstone.—On Dec. 20, 1947, at King's College Hospital, London, S.E., Frederick John Carlyle Johnstone, M.D., late Colonial Medical Service.

Jones.—On Dec. 22, 1947, Herbert Saunders Wansbrough Jones, M.B., C.M.

Masina.—On Dec. 17, 1947, at Masina Hospital, Bombay, Ardeshir Hormasji Masina, M.D., M.R.C.P., aged 36.

Mitchell.—On Dec. 18, 1947, John Malcom Lamont Mitchell, M.B., Ch.B., of 10, Claremont Gardens, Upminster.

Pilcher.—On Dec. 26, 1947, at Thirty Trees, Ashtead, Surrey, Edgar Montagu Pilcher, C.B., C.B.E., D.S.O., F.R.C.S., Major-General, late R.A.M.C., aged 82.

Ramsden.—On Dec. 23, 1947, at Briarfield, Dobcross, Oldham, Herbert Ramsden, M.D., J.P.

Robson.—On Dec. 19, 1947, at Inverness, Briton Smallman Robson, M.B., B.S., Surgeon Captain, R.N., retired.

Sealy.—On Dec. 18, 1947, at Old Orchard, Chardstock, Humfrey Newnham Sealy, M.R.C.S., L.R.C.P., Colonel, late R.A.M.C., aged 60.

Sheldon.—On Dec. 25, 1947, Arthur Izod Sheldon, M.R.C.S., L.R.C.P., Surgeon Captain, R.N., of Landrail, 1, Craneswater Park, Southsea.

Stebbing.—On Dec. 22, 1947, at 38, Telford Avenue, London, S.W., George French Stebbing, F.R.C.S., F.F.R.

Stringer.—On Dec. 13, 1947, at Port-Alberni, B.C., Wilfred Isaac Bompas Stringer, M.D., M.C.P.S.

Wagner.—On Dec. 17, 1947, at 1, Albemarle Villas, Stoke, Robert Bird Wagner, M.B., B.Ch.

Watson.—On Dec. 24, 1947, James Watson, M.B., C.M., of Hollybank, Thingwall, Wirral.

Willoughby.—On Dec. 17, 1947, at 2, Church Street, Southwell, James Frederick Digby Willoughby, O.B.E., M.R.C.S., L.R.C.P., aged 91.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Chronic Mastitis

Q.—*What treatment do you suggest for chronic mastitis, and what is your opinion of injections of testosterone propionate in these cases?*

A.—The hormone treatment of chronic mastitis is based on the view that the condition is due to excessive stimulation by endogenous oestrogens. Testosterone propionate, if given in large doses, can prevent ovarian follicle development and ovulation by inhibition of the pituitary gonadotrophic hormone secretion. Such a dosage—in the neighbourhood of 200 mg. weekly—is likely to produce hirsutism and acne. On the favourable side it results, in many cases, in relief of pain, and sometimes in disappearance or diminution of painful nodules. Smaller doses than this—for example, 25 mg. injected twice weekly—may ameliorate the symptoms of chronic mastitis without producing amenorrhoea or virilism. It is noteworthy, however, that Spence (*Lancet*, 1939, **2**, 820) found that pain was relieved in 13 of 24 patients by injection of sterile olive oil, indicating the importance of a psychological factor in some cases. Nevertheless, both he and Atkins (ibid., 1940, **2**, 412) found that benefit from androgens was probably real, although the effect was not permanent.

Tallqvist Method of Haemoglobin Estimation

Q.—*As a matter of interest, I have made a rough Tallqvist estimation of haemoglobin on my panel patients. Of 200 estimations only one is over 60%; many are as low as 40%. Can this be due to rationing?*

A.—The Tallqvist method of estimating haemoglobin is generally agreed to be grossly inaccurate, and incidentally to give low values. The method is so unreliable that it is impossible to interpret the information supplied. It seems most unlikely that anaemia is becoming widespread, since a committee of the Medical Research Council which carried out a large-scale investigation in 1943 found no apparent increase in anaemia despite rationing.

Vaginal Pruritus

Q.—*Can there be any connexion between oestrogen treatment and vaginal pruritus? A woman aged 38, living in India, has for the past year suffered from pruritus limited to a small patch of erythema on the posterior vaginal wall just internal to the carunculae hymenales. The itching is sporadic, occurring once a month and lasting about ten days, but is unconnected with menstruation. During an attack the erythema does not spread to the surrounding tissues. Glycosuria and cervical erosion have been excluded. The patient has had courses of oestrogen by injection, repeated at intervals of two to three months, for sterility. These have now been discontinued with no change in the pruritic condition. What further treatment is recommended?*

A.—Although allergic reactions to various oestrogens are described (see Zondek and Bromberg, *J. Obstet. Gynaec. Brit. Emp.*, 1947, **54**, 1) the clinical features of this case do not suggest this as a likely explanation. The strictly limited nature of the lesion prompts a search for something different from the usual causes of diffuse pruritus vulvae—for example, trichomonas vaginitis, achlorhydria, anaemia, avitaminosis—although these should be excluded. Has the possibility of self-inflicted trauma been considered? In order to establish the diagnosis and to determine the appropriate treatment it will probably be necessary to excise a small portion of the affected area for histological examination; in particular Bowen's disease (intra-epidermal carcinoma) should be kept in mind. This is rare, but the description given, although not typical, is in keeping with this diagnosis.

Occupational Leucoderma

Q.—*In March, 1941, it was reported from Washington that negro workers in tanneries noticed that the skin of their hands was turning white. This was said to be due to the presence of monobenzyl ether of hydroquinone, which was used to preserve the rubber gloves worn by the workers. I would be grateful for any concrete information about the above and any references to the literature.*

A.—Monobenzyl ether of hydroquinone (quinol) is a powerful reducing agent, and as an anti-oxidant has been used in rubbber compounding. It was the causative agent in an outbreak of occupational leucoderma among negroes working in a tannery in 1938; they wore a heavy gauntlet-type glove which had been treated with 0.2% of this anti-oxidant to preserve the rubber (Schwartz, Oliver, *et al., Publ. Hlth. Rep., Wash.*, 1940, **55**, 1111). White spots appeared on the areas of skin of the forearms and hands which were covered by the rubber gloves; there was itching with in some cases a mild dermatitis preceding the appearance of depigmentation, but there was no great discomfort or any disability. Hydroquinone monobenzyl ether is not a pigment bleach—that is, it does not decolorize melanin but simply prevents its formation. Repigmentation of the leucodermic areas followed cessation of the use of the anti-oxidant. The general health of the workers was not affected. Other references are: Schwartz, *Publ. Hlth. Bull., Wash.*, 1939, **249**, 25; Schwartz, Tulipan, and Peck, *Occupational Diseases of the Skin*, 2nd ed., 1947, 153, 451.

Inheritance of Deaf-mutism

Q.—*What are the chances of a second deaf-mute occurring in a family? The first child is a deaf-mute boy; the second is a normal boy. There is no history of deaf-mutism on the wife's side, but two cases are known on the husband's side—a male three generations back (a great-grand-uncle of the husband) and a female collateral (a direct descendant of the husband's great-grandmother). Can the chances be estimated with any degree of certainty?*

A.—Hereditary deaf-mutism is due to a recessive gene. The absence (presumably) of any extraneous cause for the child's condition and the history of the defect in the father's family leave little doubt in this particular instance. The chance that any subsequent child will be similarly affected is 1 in 4. When the time comes for the children to marry there is no reason why the deaf-mute and the normal brother should not have children. Always provided that they do not marry blood relatives or women with a family history of deaf-mutism, the chance of the defect's appearing in the next generation is very small.

Sterilization of Rubber Gloves in Midwifery

Q.—*Is it satisfactory bacteriologically to sterilize rubber gloves for use in midwifery by washing them on the hands in soap and water, drying, and then rubbing in "dettol" obstetric cream for five minutes? Will you discuss this in relation to intact gloves, patched gloves, or "holed" but unpatched gloves?*

A.—The only really satisfactory procedure is to sterilize intact gloves by boiling or autoclaving and to apply them after the usual scrubbing of the hands. Except in emergency anything short of this is indefensible. If the wearing of damaged gloves is unavoidable they should be carefully patched, and if the patches are kept to the inside there is less risk of their becoming disturbed during operations. Procedures to be adopted in emergency will vary with the circumstances, but should be worked out with the ideal in mind, and with the knowledge that rinsing in antiseptic solutions or smearing with antiseptic cream, though better than nothing, is not very efficient. One of the difficulties in removing all bacteria by washing and scrubbing the bare hands is the surface irregularities. Provided care is taken where the gloves wrinkle at the wrist, this disadvantage is to some extent minimized by thorough washing of the gloved hands. If the gloves are patched, however, this advantage is lost and the procedure becomes less efficient. In any case the gloves should not be dried afterwards unless sterile towels are available. Punctured but unpatched gloves should not be used under any circumstances.

Undulant Fever

Q.—*A veterinary surgeon working with S 19 anti-abortus vaccine developed pustules on his forearm. Later he was clinically proved to have abortus fever. Shortly afterwards his wife developed the condition and aborted. (a) Is it reasonable to suppose that the husband's infection was caused by the vaccine? (b) Is it possible that he transmitted the condition to his wife? (c) Does it follow that her abortion was caused by the infection?*

A.—(*a*) The S 19 *Brucella abortus* vaccine is living but attenuated; whether the organisms contained in it could produce infection in man is not positively known. On the other hand, their reduced pathogenicity is likely to operate in man as well as in cattle, and a veterinary surgeon is in any case much more likely to have acquired the disease in the usual way from infected animals.

(*b*) Case-to-case transmission of undulant fever has not been observed; presumably it could occur, since the organism may be found in faeces and urine. Transmission by coitus is theoretically possible, but perhaps improbable, since coitus is unlikely in the acute stage, when the organism may be found in the urinary tract. The wife, of course, may also have acquired the disease from an infected animal or from milk. Further information about dates of onset and the existence of other possible sources of infection would be necessary in elucidating this interesting occurrence.

(*c*) *Br. abortus* can cause human abortion, but there can be no proof, short of demonstrating the organism in the uterus or placenta at the time, that it did so in any particular case.

Intractable Tinnitus

Q.—*About seven months ago I developed tinnitus in my left ear; it is high-pitched and continuous, and is worse on waking. There is no pain, vertigo, or deafness, and no history of previous ear trouble. I am 50 years of age, highly strung, and a "worrier," but except for a mucoid nasal and post-nasal catarrh, particularly in the morning, I am healthy and free from any cardiovascular abnormality. Blood pressure 140/80 mm. Hg; red cell count 5.7 millions per c.mm.; haemoglobin 102%. Clinical examination of the ear shows no evidence of disease and the Eustachian tube is patent. X-ray films of the teeth and sinuses are negative, though there is an unerupted upper canine on the left side. The tinnitus is most distressing and I find it difficult to get to sleep. Bromides and phenobarbitone give me a disturbed rest and a depressing carry-over the next day. What is the cause of the condition and what is the immediate and ultimate prognosis? Is there any treatment?*

A.—Tinnitus is considered to be due to some irritation of the inner ear or auditory nerve, but in many cases the cause is not discovered, and in others the damage is irreversible, and so not amenable to treatment. All the usual causes seem to have been eliminated in this case. Lempert has described a small series of cases (*Arch. Otolaryng.*, Chicago, March, 1946) in which he divided the tympanic plexus of nerves. In most cases the tinnitus was alleviated, but the series was too small for any convincing conclusions to be drawn. Acid. hydrobrom. dil. or ammon. brom. are the most generally useful sedatives. In the present case the tinnitus will probably be permanent but become more bearable as time goes on.

NOTES AND COMMENTS

Food Allergy.—Mr. ERIC C. WOOD, Ph.D. (London, W.), writes: May I add one further comment on the subject of sensitivity to egg in a child (Nov. 29, 1947, p. 896)? It is far more likely if a child is genuinely sensitive to egg that the allergy is to egg *white* rather than egg *yolk*. Marriott, W. M., and Jeans, P. C., in their book *Infant Nutrition*, London (3rd edition, 1942, pp. 224 and 225), say: "A fear that formerly existed that the effect of egg in early infancy might lead to the development of sensitivity to egg protein seems unfounded in the light of extended clinical experience in instances in which only the yolk has been fed. It is desirable that the egg be cooked." While they suggest that egg yolk may be added to the diet of the infant at as early an age as three months, they state that whole egg may be given toward the end of the first year. "The chief reason it is not commonly given earlier is the possibility that sensitivity to protein of egg white may develop as a result of the feeding. . . . At whatever age the feeding of egg white is started, it should be given cautiously and in small amounts at first." The point is of importance, since egg yolk is a most important food providing valuable quantities of many essential nutrients, not the least important of which is iron. Moreover, most babies find egg yolk extremely palatable. It would be a great pity if babies were deprived of a toothsome delicacy which is also an excellent food because they are allergic to egg albumen.

Ringworm of Scalp.—Col. W. H. CRICHTON, C.I.E., I.M.S. (ret.), writes from Sittingbourne, Kent, with reference to Dr. J. T. Duncan's letter (Nov. 29, 1947, p. 896): The causative fungus in all the cases I had in North Devon was reported by the Devon County Laboratory to be the *Microsporum felinum*. I refer to cases which occurred between February and May, 1947.

Superfluous Hair.—J. M. writes: The problem of superfluous hair becomes of the utmost importance to some women. Personally, I greeted the original *B.M.J.* answer (Nov. 15, p. 805) with approval as giving sensible and practical advice. To my mind it is quite impractical to advise electrolysis as a routine measure and usually unnecessary, except in those cases where there are a small number of exceedingly stiff hairs. The commonest problem arises with a woman, say in the early thirties, who feels that she has become unsightly through a generalized growth of hair. Clearly the trouble will be progressive, and to embark on electrolysis would be endlessly tedious and costly. Her choice of methods is either depilatory wax or an occasional shave. The advantage that wax offers is that since the hair is pulled out from the follicle the new growth of hair, when after several days it comes through, is soft and quite unlike the cut-off, bristly quality of a shaved hair. Most women who begin with depilatory wax in the twenties or thirties do not ever require to use it more than once in several days; the process takes some five or ten minutes, and the results are frequently perfect. On the other hand, shaving may sometimes become a daily necessity for a fastidious woman; but even so it is always wise to assure her that her growth will never become that of the average masculine skin. To my mind it is the way in which advice is administered which is the important factor; many middle-aged women feel that they are the only sufferers, and experience intense humiliation. They are greatly relieved to have it pointed out that their friends with immaculate skin have probably been using wax for a decade and that it is high time that they themselves followed suit. The really difficult part of this procedure is relieving the patient of her humiliation and her masochistic impression that she must expect to endure and suffer!

Constipation in an Infant.—Dr. ANN MOWER WHITE (London, W.) writes: I have only just seen the question and answer (Nov. 29, 1947, p. 896) about "Constipation in an Infant," and I am rather surprised at the reply. In the first place the questioner does not state whether the 4-month-old male infant is breast- or artificially fed. In a breast-fed baby an interval of seven days between bowel actions is not at all uncommon, and may be called "false" constipation in contradistinction to "true" constipation, when the stools are infrequent and hard. For "false" constipation no treatment is required beyond reassuring the mother that her milk is suiting her baby so well that there is little rubbish to pass out. If more active advice is needed, she should be told to give the baby more free kicking exercise with napkin removed and to give more water to drink in the daily routine. In an artificially fed baby "true" constipation is a more likely occurrence. The psychological trauma likely to be incurred by the daily anal insertion of a soap stick or a vaselined glass rod (as advised in the answer to the question) is a remedy fraught with too grave a risk to allow any mother to use it. More sugar added to the feeds, more water during the day, and a mild laxative such as milk of magnesia would be the more harmless procedure.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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